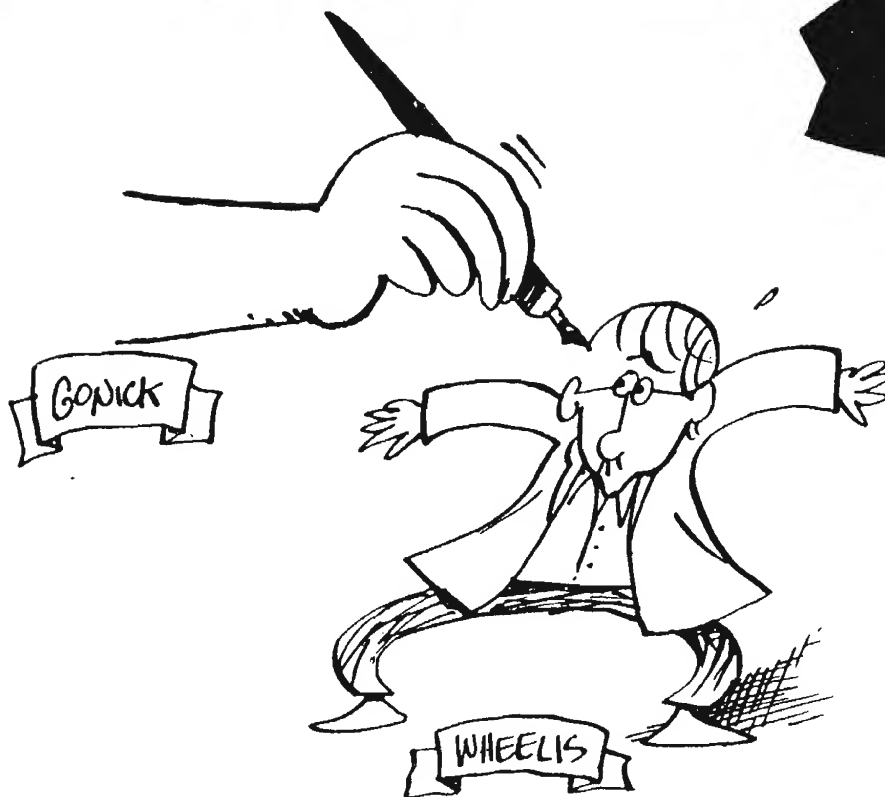


THE CARTOON GUIDE TO GENETICS

updated
edition



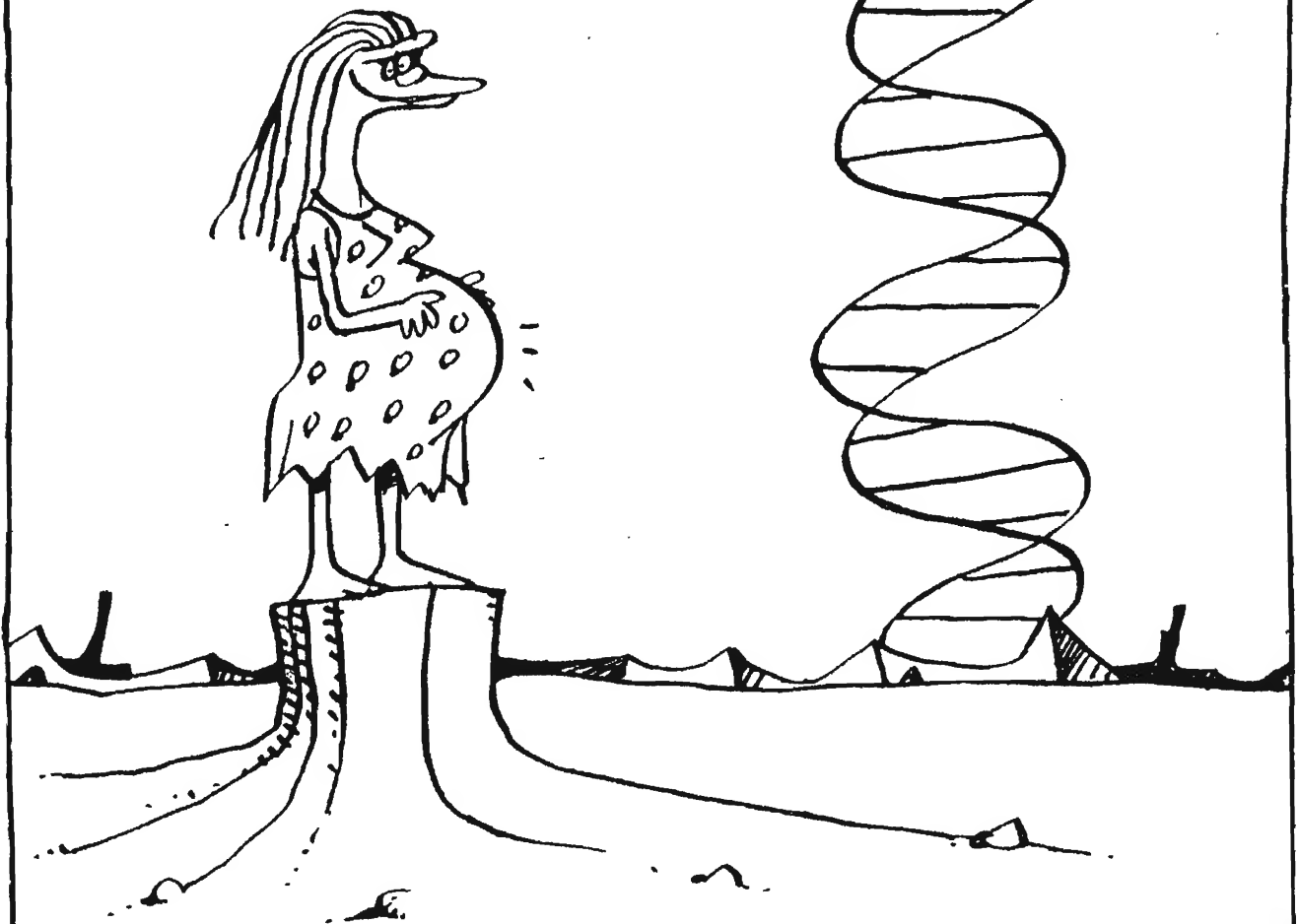
**LARRY GONICK
& MARK WHEELIS**



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THE CARTOON GUIDE TO **GENETICS**

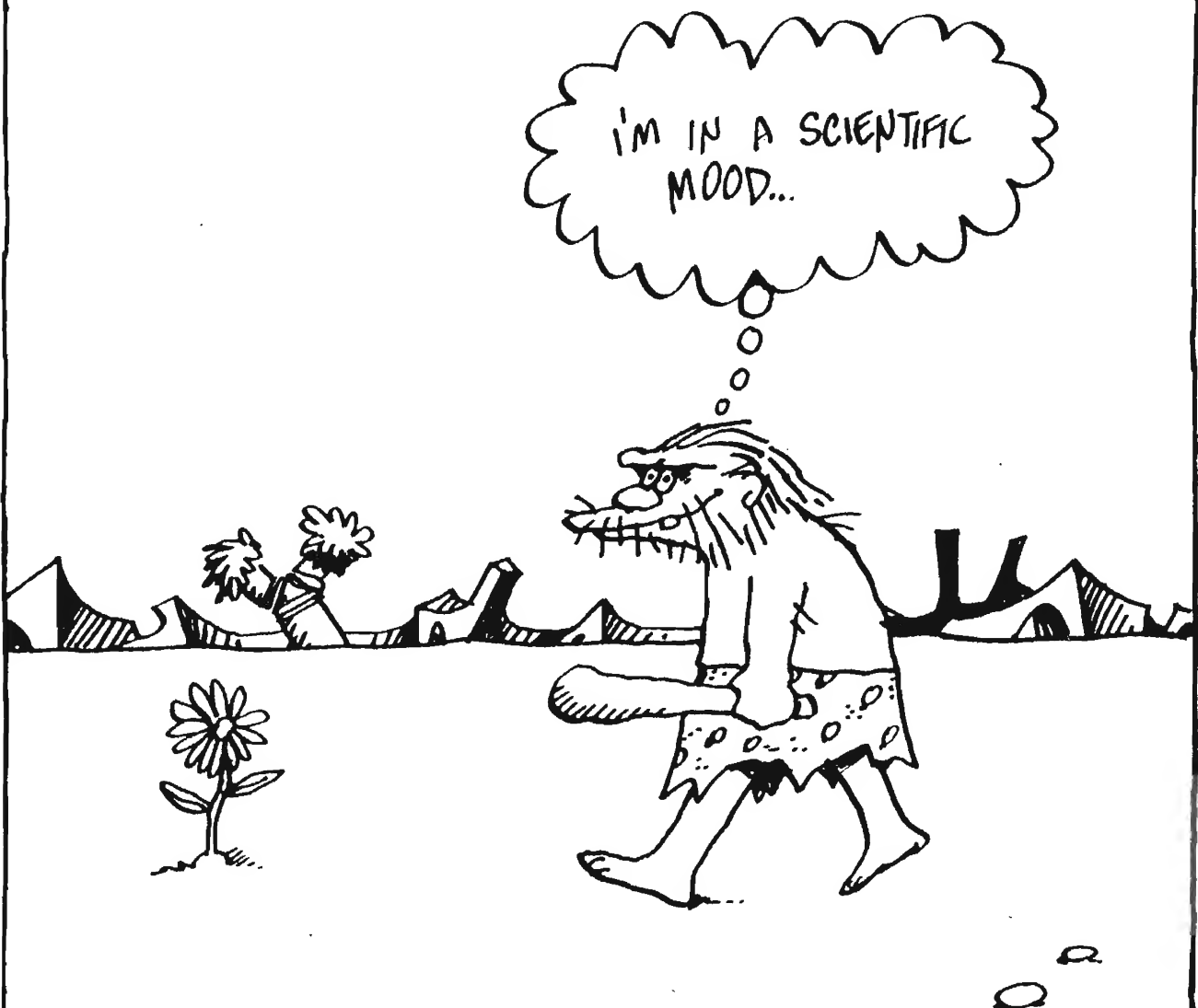
TO REPRODUCTION,
WITHOUT WHICH
OUR SUBJECT,
OUR AUTHORS,
AND OUR READERS
WOULD HAVE BEEN
IMPOSSIBLE...



**grüek*

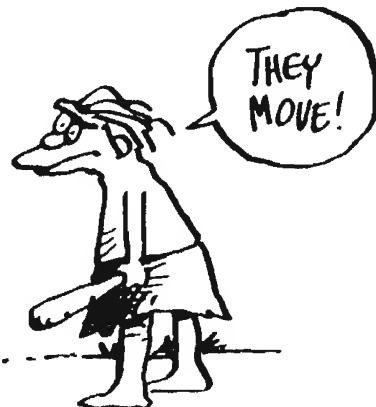
IN ANCIENT TIMES...

OUR ANCESTORS
HAD A FIRST-HAND
KNOWLEDGE OF
NATURE. IN THOSE
DAYS, EVERYONE WAS
A BIOLOGIST, AND
THE WORLD WAS
A CLASSROOM !!



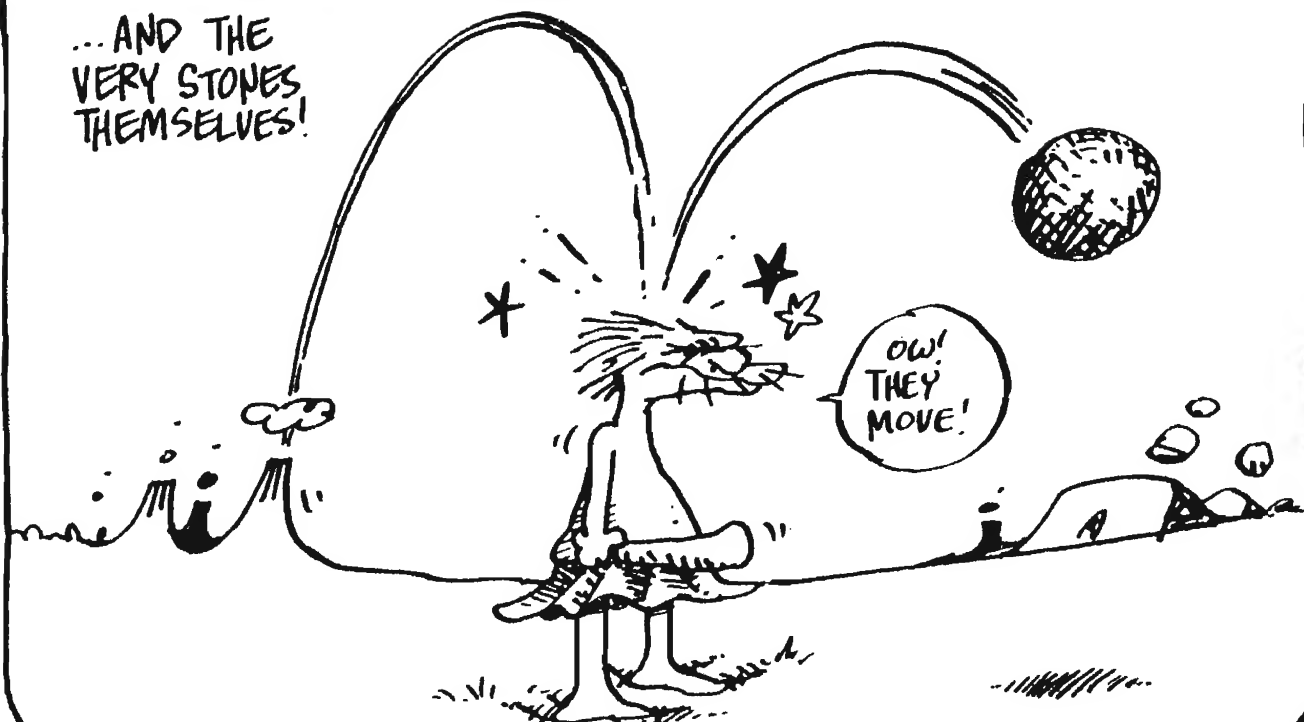
IN THEIR EARLIEST GLIMMERINGS OF THOUGHT, IT'S SAID, PEOPLE MADE NO DISTINCTION BETWEEN LIVING AND NON-LIVING THINGS. EVERYTHING WAS SUPPOSED TO BE ALIVE, A FIT SUBJECT OF "BIOLOGICAL" RESEARCH.

THIS INCLUDED TREES...



...ANIMALS...

...AND THE VERY STONES THEMSELVES!



IN THE COURSE OF THEIR STUDIES, OUR ANCESTORS MUST HAVE NOTICED AN OBVIOUS FACT: SOME THINGS TENDED TO REPRODUCE THEMSELVES.

PEOPLE
DID IT...



...MAMMOTHS
DID IT...



...AND, TO THE
PRIMITIVE
MIND, IT MAY
WELL HAVE
SEEMED THAT
EVEN ROCKS
COULD "GIVE
BIRTH" TO
LITTLE PEBBLES!



MANY SCHOLARS BELIEVE THAT PRIMITIVE PEOPLE SAW NO CONNECTION BETWEEN REPRODUCTION AND SEX. THE NINE MONTHS BETWEEN CONCEPTION AND BIRTH WAS SUPPOSEDLY ENOUGH TO STYMIE THE SMARTEST STONE-AGER... AND WHAT DOES SEX HAVE TO DO WITH THE REPRODUCTION OF ROCKS??!

FOR WEEKS I'VE BEEN WATCHING, AND I DON'T THINK THEY DO IT...



WE MUST ADMIT, THIS THEORY LEAVES US SLIGHTLY SKEPTICAL. IT SEEMS POSSIBLE THAT MEN MIGHT HAVE MISSED THE CONNECTION, BUT COULD WOMEN HAVE OVERLOOKED WHAT WAS HAPPENING TO THEIR OWN BODIES??!

EVER NOTICE ANYTHING FUNNY ABOUT BABIES AND SEX?

YES... YOU CAN'T HAVE ONE WITHOUT THE OTHER...



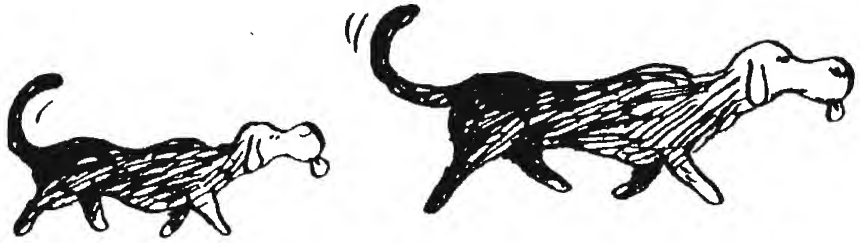
C'MON... DON'T BE SHY...

ENLIGHTENMENT CAME,
ACCORDING TO THIS THEORY,
WHEN PEOPLE FIRST
DOMESTICATED ANIMALS—
AND SAW THEIR REPRODUCTIVE
CYCLE CLOSE-UP AND OFTEN:
MATING IN ONE SEASON,
BIRTH IN ANOTHER.



IT MUST HAVE COME
AS A GREAT SHOCK
TO DISCOVER THAT
MEN HAD SOMETHING
TO DO WITH MAKING
BABIES... IT'S SAID
TO HAVE CAUSED
BIG CHANGES IN
SOCIETY, SUCH AS
FATHER'S' DAY,
PATERNITY SUITS,
MARRIAGE, AND THE
PATRIARCHY — BUT THIS
IS A BIOLOGY BOOK,
AND WE WON'T GO
INTO ALL THAT...

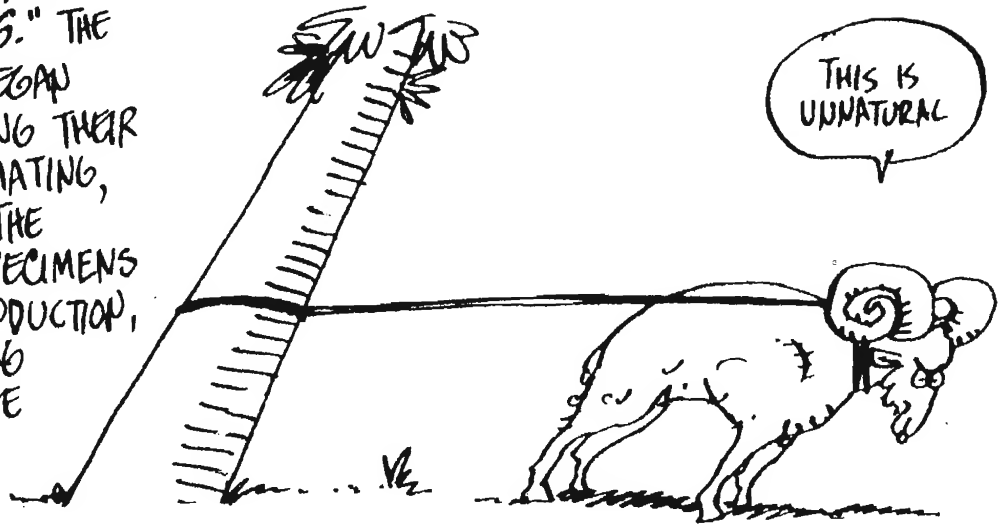
ALONG WITH THIS
CAME THE NOTION
THAT LIKE
BEGETS LIKE—
THE FIRST REALLY
GENETIC IDEA..



AND SO BEGAN

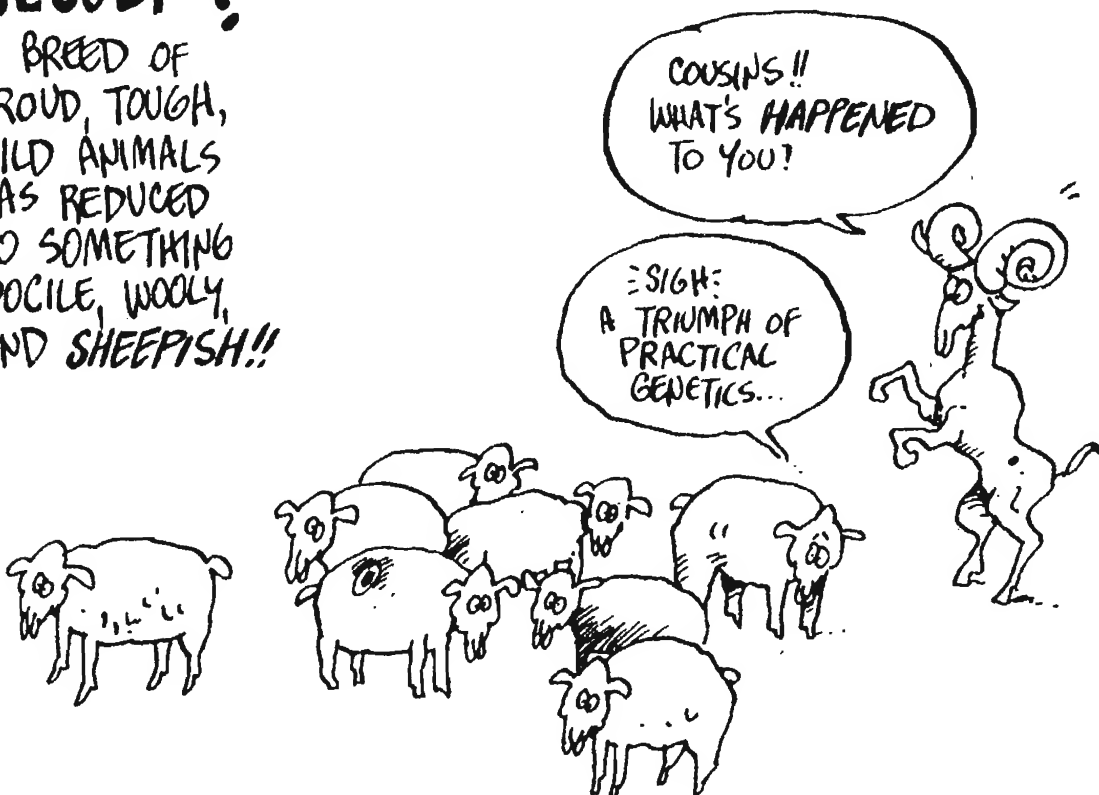
PRACTICAL GENETICS,

OR "SELECTIVE
BREEDING." THE
HERDERS BEGAN
CONTROLLING THEIR
ANIMALS' MATING,
CHOOSING THE
"BEST" SPECIMENS
FOR REPRODUCTION,
AND GETTING
RID OF THE
"WORST."

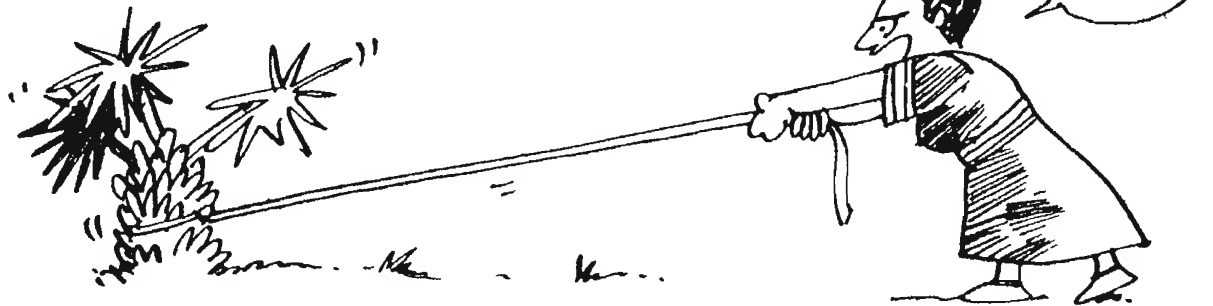


RESULT ?

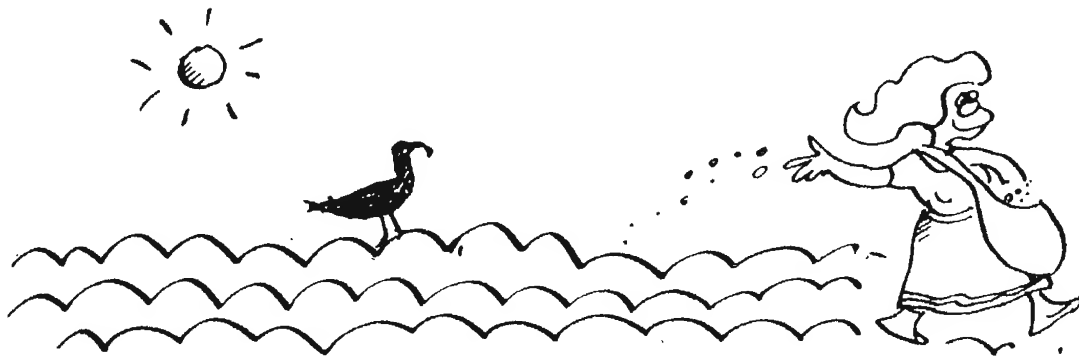
A BREED OF
PROUD, TOUGH,
WILD ANIMALS
WAS REDUCED
TO SOMETHING
DOCILE, WOOLLY,
AND SHEEPISH!!



AT THE SAME TIME, PEOPLE WERE DOMESTICATING PLANTS:



EARLY FARMERS USED THE SAME METHODS AS THE ANIMAL HERDERS, WEEDING OUT UNDESIRABLE STRAINS AND PLANTING ONLY THE BEST SEEDS.



THIS HAPPENED ALMOST EVERYWHERE IN THE WORLD: SCRAWNY WEEDS AND GRASSES WERE GRADUALLY TURNED INTO RICH, PRODUCTIVE CROPS. RICE, WHEAT, BARLEY, AND DATES IN ASIA; CORN, SQUASH, TOMATOES, POTATOES, AND PEPPERS IN AMERICA; YAMS, PEANUTS, AND GOURDS IN AFRICA — ALL SPECIALLY IMPROVED BY HUMANS !!



PLANTS HAVE
SEX TOO... THEY'RE
JUST LESS
NOISY ABOUT IT
THAN ANIMALS.

EARLY ON,
PEOPLE NOTICED
THE IMPORTANCE
OF **POLLINATION**:
POLLEN DUST
MUST LAND ON
A FLOWER
BEFORE IT CAN
PRODUCE
FERTILE SEEDS.

DAUGHTER, LET
ME TELL YOU
ABOUT THE BIRDS
AND THE HUMANS...

I ALREADY
LEARNED IT
IN THE GUTTER
...



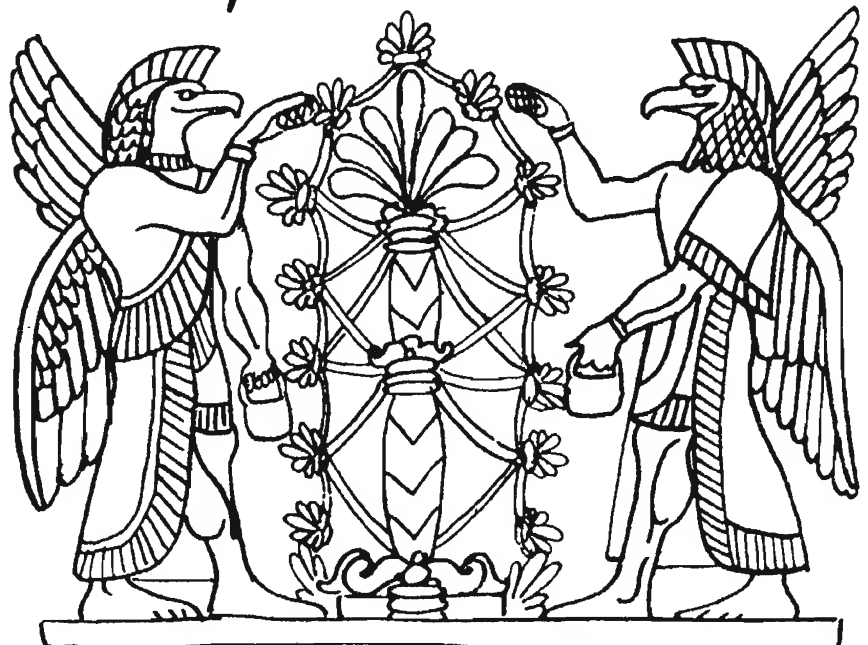
HOWEVER -

THE EARLY
FARMERS REALLY
DIDN'T KNOW
WHY POLLINATION
WORKED - SO
THEY ADDED
SOME **MAGIC**,
JUST TO BE
ON THE SAFE
SIDE...

THESE ARE
ASSYRIAN PRIESTS,
POLLINATING
A DATE PALM,
AROUND 800 B.C.

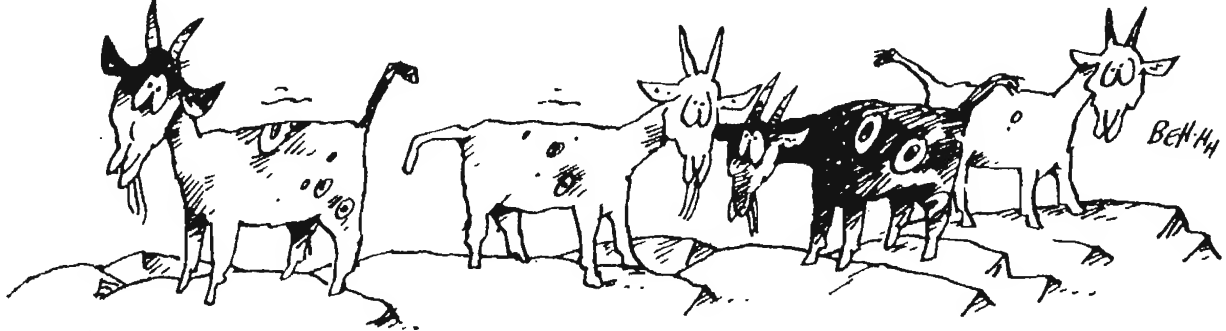
WHAT WOULD
HAPPEN IF WE
DIDN'T WEAR THESE
BIRD SUITS?

≡ PUK PUK ≡
WHAT BIRD
SUITS, HUMAN?



THIS COMBINATION OF SCIENCE AND MAGIC IS NICELY ILLUSTRATED BY A BIBLE STORY... GENESIS, CHAPTER 30, OR...

THE CASE OF JACOB'S FLOCK



IN THIS STORY, THE PATRIARCH JACOB AGREES TO TEND THE FLOCK OF HIS FATHER-IN-LAW LABAN. AS PAYMENT, JACOB MAY TAKE ALL THE "SPECKLED AND SPOTTED" ANIMALS FOR HIMSELF, WHILE LABAN KEEPS THE PURE BLACK ONES. THE TWO GROUPS ARE NOT TO INTERBREED.



THE BIBLE DESCRIBES JACOB'S FERTILITY MAGIC CAREFULLY: HE STRIPPED THE BARK FROM WILLOW RODS, AND "MADE THE WHITE APPEAR WHICH WAS IN THE RODS", THEN SET THEM NEAR THE WATERING HOLE.

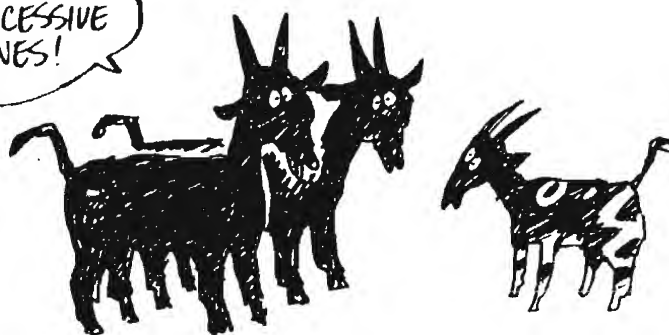


THE IDEA BEHIND JACOB'S ACTION IS THAT **LIKE BEGETS LIKE**: BY SHOWING THE WHITE IN THE WILLOW RODS, HE WAS TRYING TO BRING OUT THE WHITE IN LABAN'S BLACK ANIMALS !! THIS IS CALLED **SYMPATHETIC MAGIC**...



THE POINT, GENETICALLY SPEAKING, IS THIS: IN FACT, THE PURE BLACK ANIMALS **BORE SPECKLED OFFSPRING** —AND SO JACOB'S FLOCK INCREASED! WHY??

RECESSIVE GENES!



WE'LL COME BACK TO THIS LATER!

HERE WE SEE ACCURATE GENETIC OBSERVATION SIDE-BY-SIDE WITH A NEAR TOTAL LACK OF UNDERSTANDING.

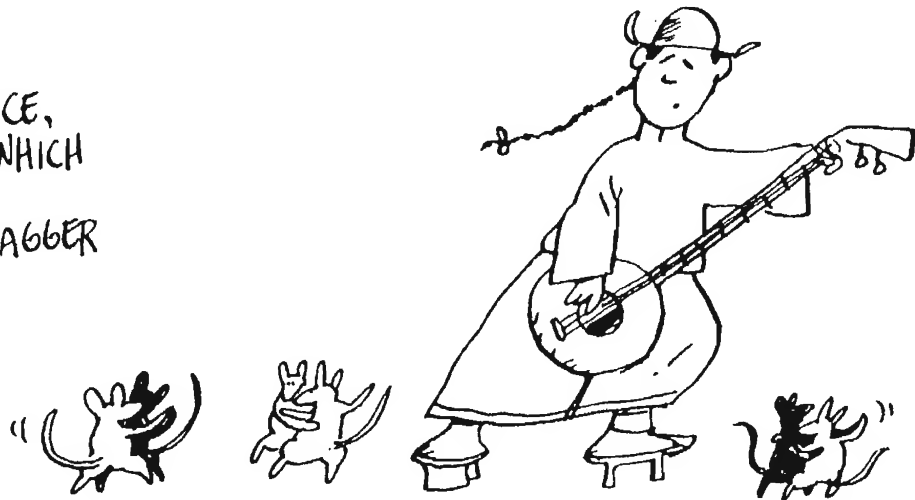
LABAN CERTAINLY DIDN'T GET IT!!

YOU GET MY GOAT!!



SOME OTHER GENETIC ITEMS FROM ANCIENT HISTORY:

THE CHINESE
DISCOVERED
"WALTZING" MICE,
A MUTATION WHICH
CAUSES THE
ANIMAL TO STAGGER
AROUND IN
CIRCLES.



THE HINDUS OBSERVED
THAT CERTAIN DISEASES
MAY "RUN IN THE
FAMILY." MOREOVER,
THEY CAME TO BELIEVE
THAT CHILDREN
INHERIT ALL THEIR
PARENTS' CHARACTERISTICS.
"A MAN OF BASE
DESCENTS CAN NEVER
ESCAPE HIS ORIGINS,"
SAY THE LAWS OF
MANU...

THE
BASIS
OF THE
CASTE
SYSTEM!



XENOPHON, A GREEK,
HAD THIS TO SAY
ABOUT BREEDING
HOUNDS:

"GET A GOOD
DOG FOR THE
PURPOSE."



SEVERAL OTHER GREEKS, THINKING MORE DEEPLY THAN XENOPHON, DEVELOPED THE FIRST REAL THEORIES OF **HEREDITY**— IN OTHER WORDS, THEY ADDRESSED THE QUESTION: "WHY DO CHILDREN RESEMBLE THEIR PARENTS?"



ACTUALLY, ONE PHILOSOPHER, **SOCRATES**, WONDERED WHY THEY SOMETIMES **DON'T**... HE USED TO SAY THAT THE SONS OF GREAT STATESMEN WERE USUALLY LAZY AND GOOD FOR NOTHING... WE SHOULD ALWAYS BEAR THIS IN MIND, THAT NOT EVERY QUALITY IS INHERITED...

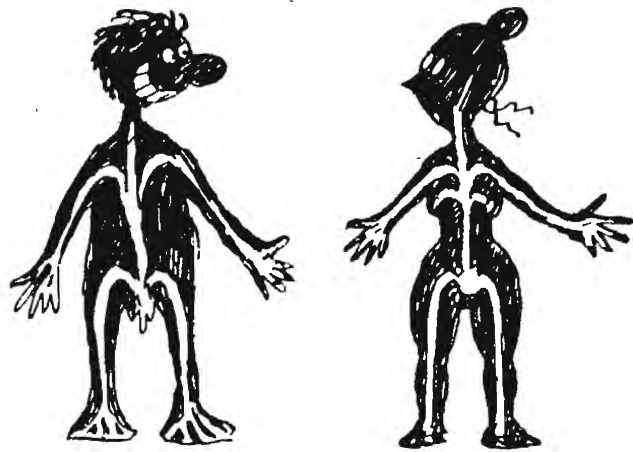
UNFORTUNATELY, BY SUCH UNFLINCHING HONESTY, **SOCRATES** PROVOKED THE **ATHENIANS** TO PUT HIM TO DEATH...



THE MOST COHERENT
GREEK THEORY OF
HEREDITY WAS THAT
OF THE FAMOUS DOCTOR
HIPPOCRATES.



HIPPOCRATES
RECOGNIZED THAT
THE MALE CONTRIBUTION
TO A CHILD'S
HEREDITY IS CARRIED
IN THE SEMEN.
BY ANALOGY, HE
ASSUMED THERE WAS
A SIMILAR FLUID IN
WOMEN.

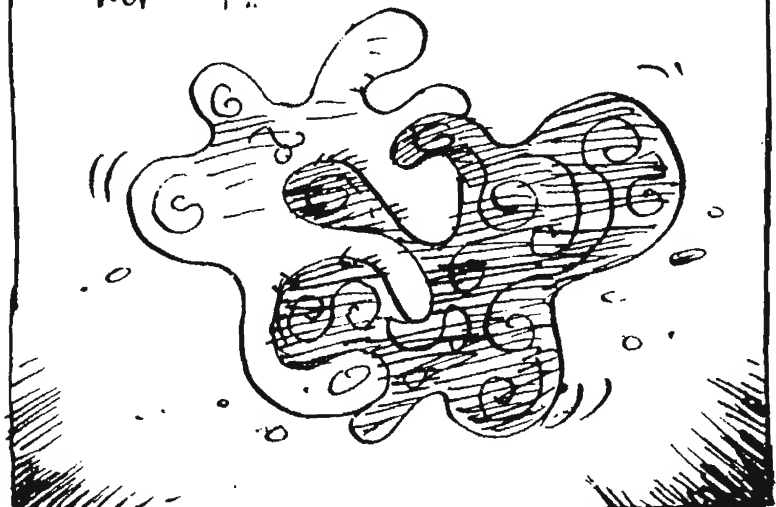


THESE FLUIDS, HE REASONED,
WERE MADE THROUGHOUT THE
BODY, AND THEN COLLECTED IN THE
REPRODUCTIVE ORGANS.

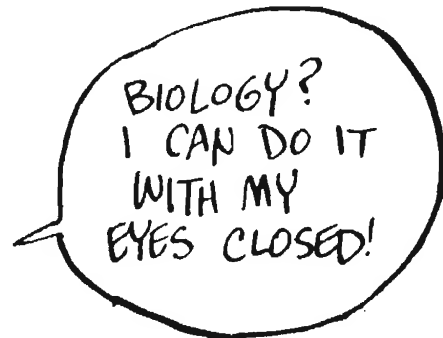


THE SEMEN
FROM THE FINGERS
HAD THE MATERIAL
TO MAKE MORE
FINGERS; THAT
FROM THE HAIR
MADE HAIR, ETC
ETC ETC...

AT CONCEPTION, A SORT OF
BATTLE OF THE FLUIDS TOOK PLACE,
AND WHETHER THE CHILD'S HANDS
WERE MORE LIKE MOM'S OR DAD'S
DEPENDS ON WHOSE FINGER-SEMEN
WON OUT!!



UNFORTUNATELY, THE GREEK WHOSE IDEAS MOST INFLUENCED LATER GENERATIONS WAS NOT HIPPOCRATES, BUT **ARISTOTLE**. WHEN IT CAME TO SCIENCE, ARISTOTLE NEVER LET HIS IGNORANCE STAND IN THE WAY OF HIS THEORIES!!



ARISTOTLE — CALLED "THE PERIPATETIC" BECAUSE HE PACED WHILE HE LECTURED — BELIEVED THAT ALL INHERITANCE CAME FROM THE **FATHER**... THE MALE SEMEN, HE SAID, DETERMINED THE BABY'S FORM, WHILE THE MOTHER MERELY PROVIDED THE MATERIAL FROM WHICH THE BABY WAS MADE...



YES, THERE WAS NO GETTING AROUND IT... THIS SEEMED TO IMPLY THAT ALL CHILDREN OUGHT TO BE BOYS... WHO KNOWS? MAYBE THIS REVEALED SOME SUBCONSCIOUS WISH OF ARISTOTLE'S... THE ANCIENT GREEKS DID VALUE BOYS MORE HIGHLY THAN GIRLS.



IN MY VERSION OF THE IDEAL STATE, ALL PHILOSOPHERS WOULD BE REQUIRED TO GET PREGNANT, AT LEAST ONCE...

BUT THE PHILOSOPHER COULD HARDLY IGNORE THE EXISTENCE OF FEMALE BABIES. HE PATCHED UP HIS THEORY BY DECLARING THEY WERE CAUSED BY "INTERFERENCE" FROM THE MOTHER'S BLOOD.



AND NOW, ON TO PHYSICS...

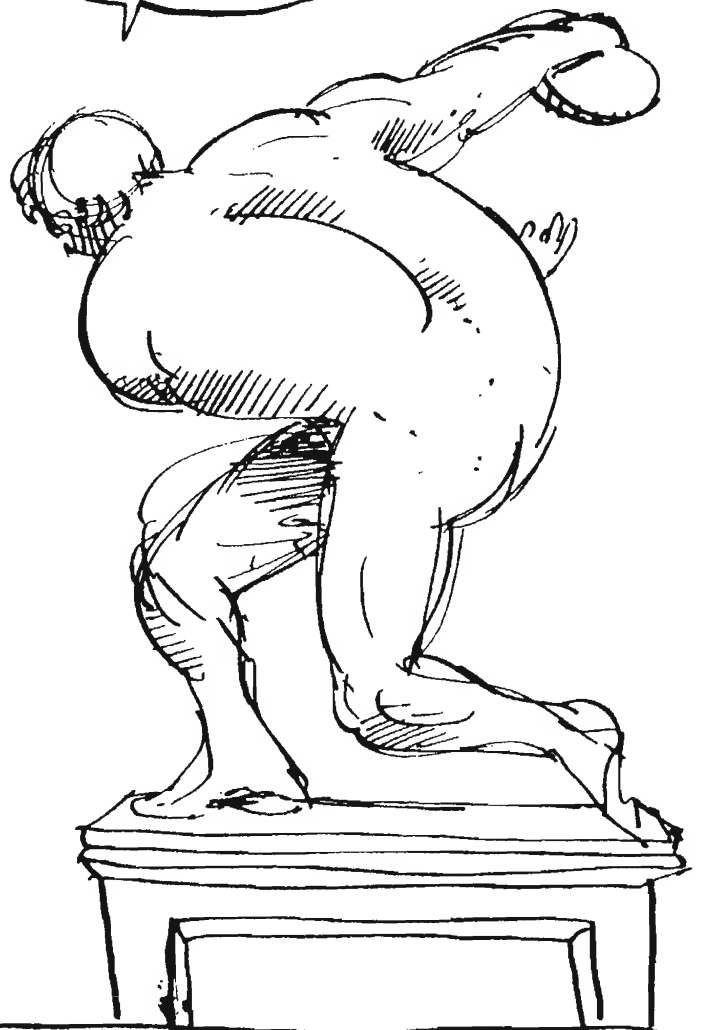
WHOSE FLUIDS
MADE MY SPECKLES?



A FINE THEORY ... EXCEPT
THAT IT DOESN'T ACCOUNT
FOR CHILDREN WHO DIFFER
FROM **BOTH** PARENTS!
BROWN-EYED PEOPLE OFTEN
HAVE BLUE-EYED BABIES,
AND DON'T FORGET JACOB'S
SPECKLED GOATS.

ONE PHILOSOPHER,
EMPEDOCLES,
THOUGHT THIS
MIGHT RESULT
FROM THE
MOTHER'S
GAZING
LONGINGLY
AT STATUES
DURING
PREGNANCY.

WHAT'S WRONG,
LADY? LOST
YOUR MARBLES?



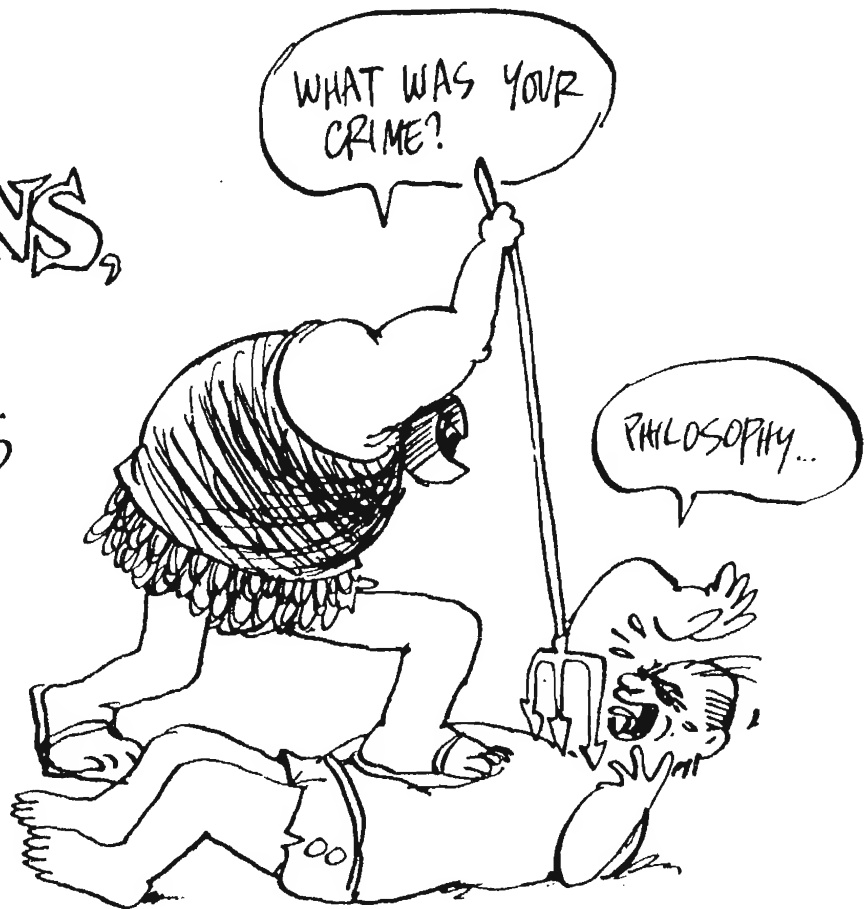
GREEK CIVILIZATION MAY HAVE PERISHED, BUT...

SCIENCE MARCHES

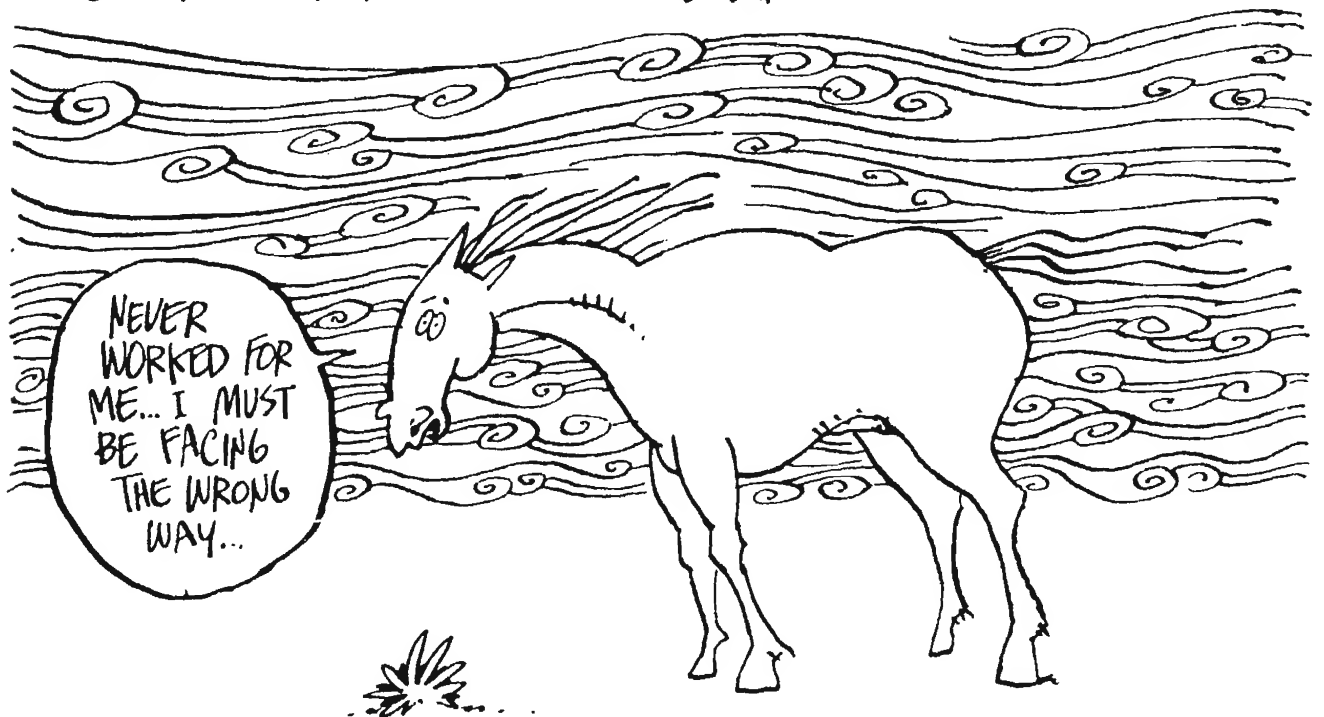
ON!



THE GREEK
MANTLE PASSED
TO THE
ROMANS,
WHO HAD
LITTLE TASTE
FOR PHILOSOPHY...
THEY PREFERRED
THE TECHNOLOGY
OF DEATH
TO THE
SCIENCE OF
LIFE.

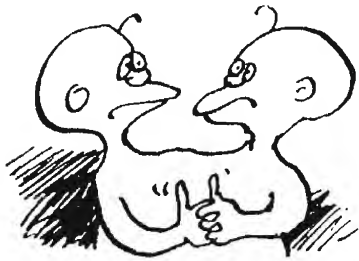


THE ONLY GENETIC IDEA THEY ADDED WAS THAT MARES
COULD BE FERTILIZED BY THE WIND...

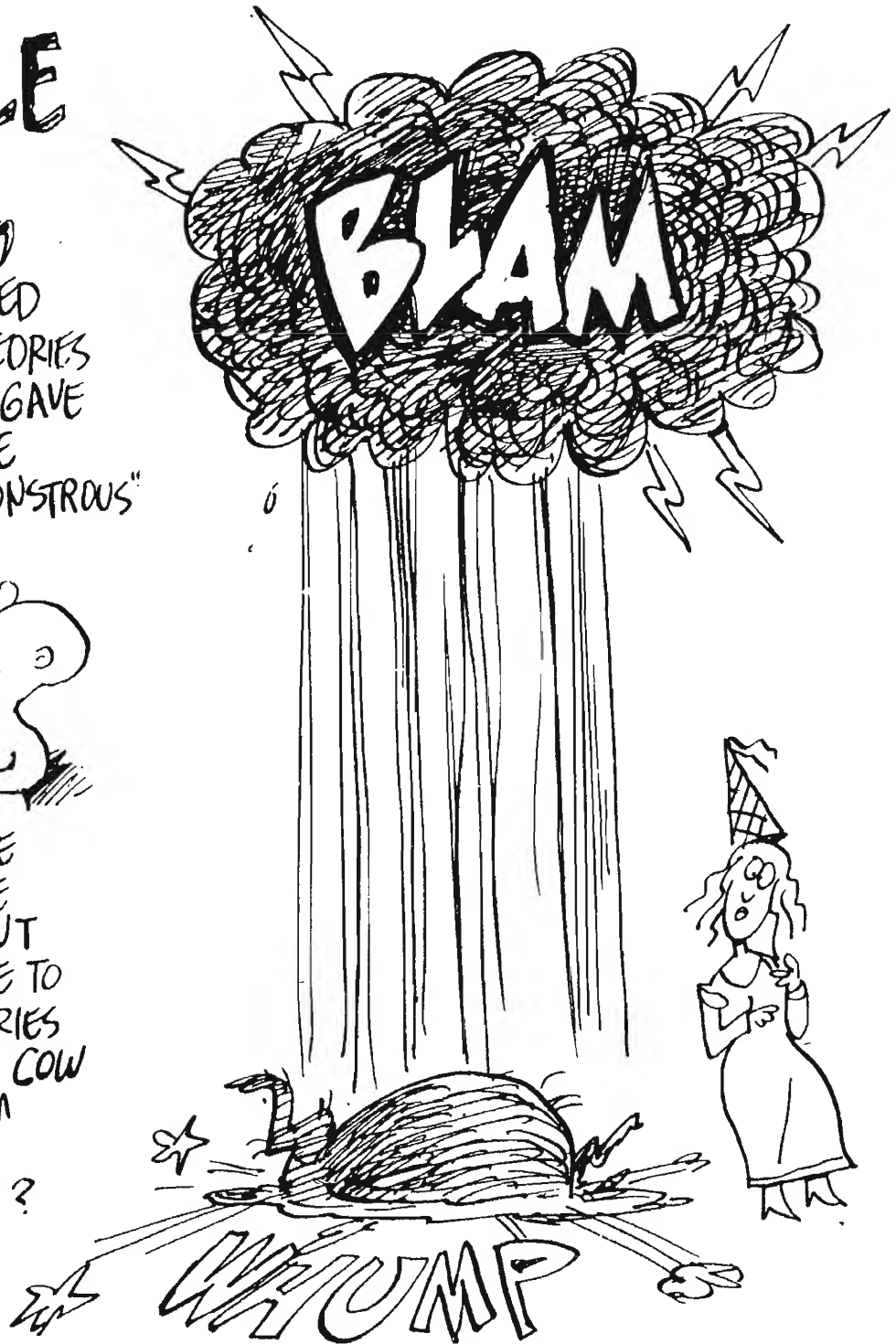


IN THE MIDDLE AGES,

SCIENCE FADED
FURTHER... THEORIES
OF HEREDITY GAVE
WAY TO MERE
LISTS OF "MONSTROUS"
BIRTHS...



SOME OF THESE
MAY WELL BE
GENUINE — BUT
WHAT ARE WE TO
MAKE OF STORIES
LIKE HALF A COW
FALLING FROM
HEAVEN IN A
THUNDERCLAP?



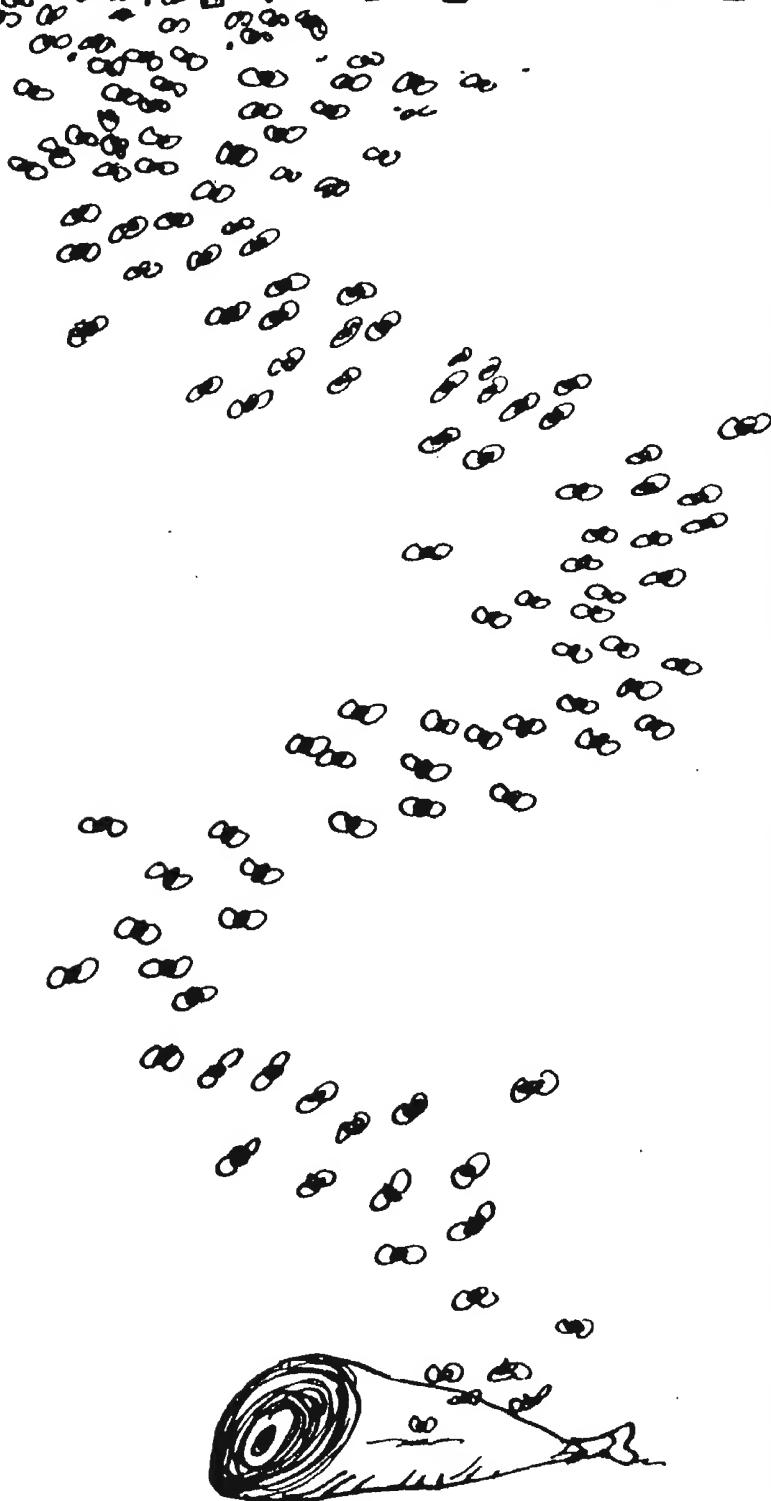
THERE'S ALWAYS THE
CHANCE IT WAS JUST
A TALL TALE... OR
SOMEONE'S IDEA OF
A JOKE...



YES... REMINDS
ME OF THE ONE
ABOUT THE
PRIORRESS, THE
ARCHDEACON,
AND THE
TWO-HEADED
SWINE...

ONE MEDIEVAL IDEA ESPECIALLY
IMPEDED UNDERSTANDING. IT WAS CALLED:

SPONTANEOUS GENERATION



IT'S
COMMON
SENSE!



ORIGINATING
WITH THE GREEKS,
THIS WAS THE
BELIEF THAT
LIVING
ORGANISMS
COULD ARISE
("SPONTANEOUSLY")
FROM NON-
LIVING MATTER.

MAMA!



MAGGOTS WERE
SUPPOSED TO COME
FROM DECAYING
MEAT... HORSEHAIR
TURNED INTO
WORMS... AND
FROGS, MICE, AND
BUGS WERE
NOTHING BUT SLIME
COME TO LIFE!!

YOU CAN'T
TELL ME
OLD
ARMOR
DOESN'T
BREED
FLEAS!



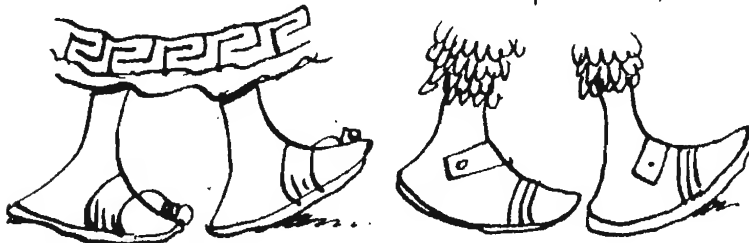
IT'S NOT HARD TO
IMAGINE WHY
SPONTANEOUS
GENERATION SEEMED
PLAUSIBLE:
IN A WORLD
WHERE SLIME
WAS COMMON,
ONE SAW IT
HAPPEN
EVERY DAY!

YOU SEE HOW BELIEF IN SPONTANEOUS
GENERATION CONFLICTS WITH
"GENETIC" THINKING? IF A FROG
COMES FROM SLIME, IT
DOESN'T MAKE MUCH
SENSE TO TALK ABOUT
INHERITED QUALITIES,
DOES IT??

NOT MUCH
FAMILY RESEM-
BLANCE, IS
THERE?



BUT - AS WE MENTIONED, SCIENCE MARCHES ON...



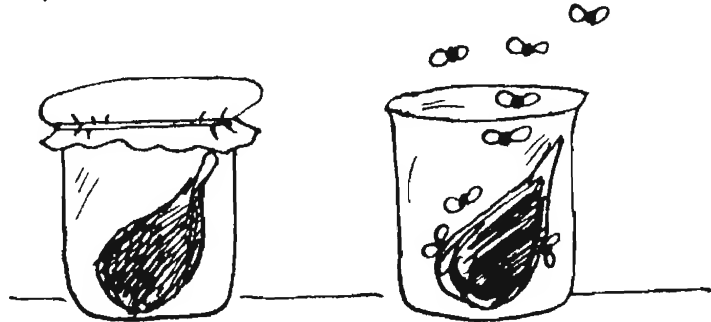
AND IN THE 17TH
CENTURY, A SIMPLE
EXPERIMENT
SUCCESSFULLY
CHALLENGED
SPONTANEOUS
GENERATION...

THE ELEGANT
DEMONSTRATION
WAS PERFORMED
BY THE
ITALIAN
FRANCESCO
REDI...

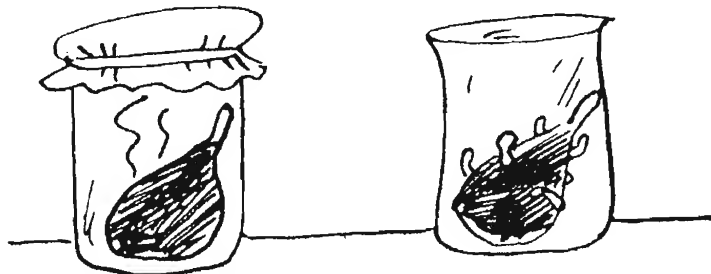


WHEN
THE TIME
IS RIGHT,
THE MAP
MUST
BE
REDI!

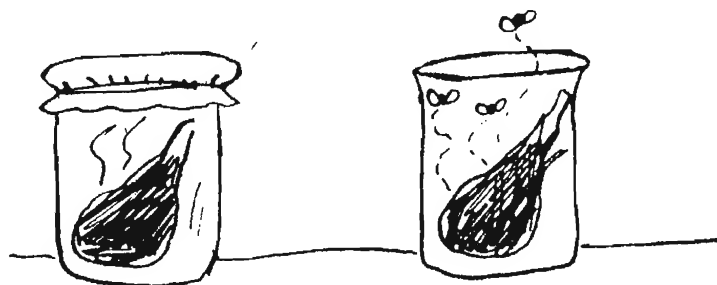
REDI PLACED PIECES OF FRESH
MEAT IN JARS... SOME OF THE JARS
HE CAPPED TIGHTLY WITH CHEESE-
CLOTH, WHILE LEAVING THE REST
OPEN TO THE FLIES...



AFTER SOME TIME HAD PASSED,
REDI FOUND MAGGOTS ONLY IN
THE OPEN JARS.

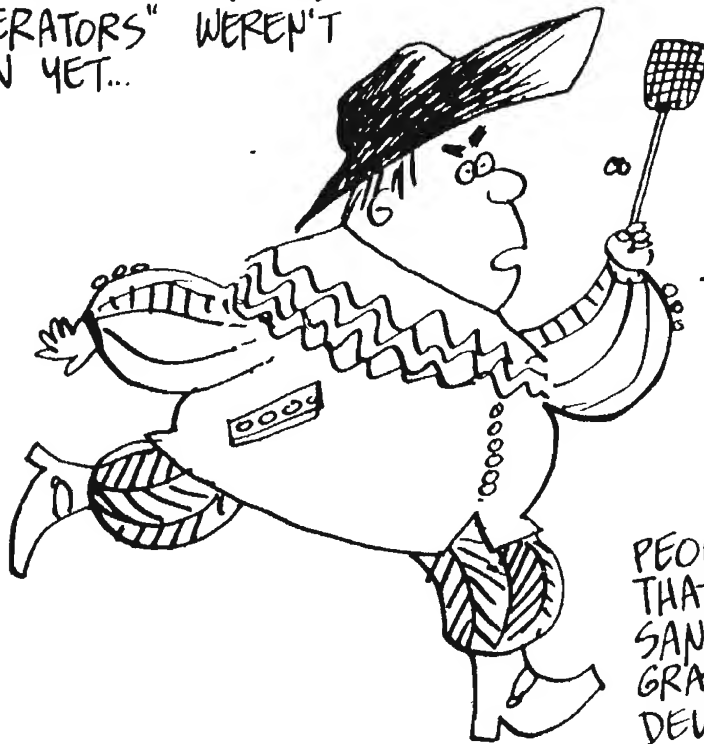


THE MAGGOTS GREW, STIFFENED INTO
COCOONS, AND FINALLY EMERGED AS
FULLY FORMED FLIES!



THUS, REDI HAD SHOWN THAT
MAGGOTS COME FROM FLIES, AND
FLIES COME FROM MAGGOTS.
NOTHING VISIBLE HAD BEEN
"SPONTANEOUSLY GENERATED" FROM
THE ROTTING MEAT!!

BUT THE "SPONTANEOUS
GENERATORS" WEREN'T
DOWN YET...



SO-WE WERE
WRONG ABOUT
FLIES... SO
WHAT?

PEOPLE STILL BELIEVED
THAT FLEAS CAME FROM
SAND, WEEVILS FROM
GRAIN, EELS FROM THE
DEW, ETC, ETC, ETC...

FLEAS, EELS, AND
WEEVILS, IN TURN,
WERE DISPOSED OF
BY ANTON VAN
LEEUVENHOEK
("LAY-VEN-HOOK"), AN
AMATEUR DUTCH
SCIENTIST AND THE
FIRST TO MAKE
SYSTEMATIC USE
OF THE
MICROSCOPE.



WHERE DO
HUMANS COME
FROM?

HOSPITALS



USING HIS SIMPLE
INSTRUMENT — JUST
AN EXCELLENT EYEPiece
REALLY — LEEUWENHOEK
FOLLOWED THE LIFE
HISTORIES OF VARIOUS
SMALL CREATURES.
HIS TREATISE ON
THE FLEA IS A
CLASSIC !!

"THIS MINUTE AND
DESPISED CREATURE,"
[HE WROTE] "IS ENDOWED
WITH AS GREAT A
PERFECTION IN ITS KIND
AS ANY LARGE ANIMAL."



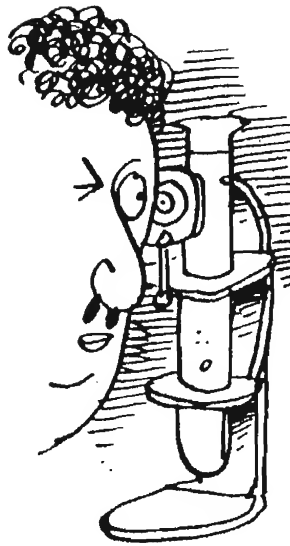
HE DISCOVERED THAT FLEAS, LIKE FISH, DOGS, AND
HUMANS, WERE **SEXUAL BEINGS!**

MARK MY WORDS:
FREE INQUIRY CAN
ONLY LEAD TO
FREE LOVE...



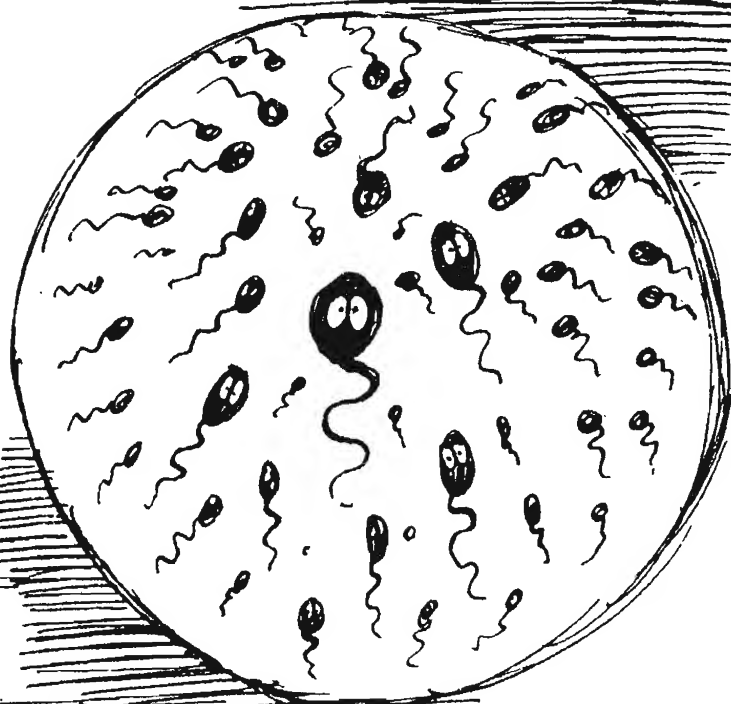
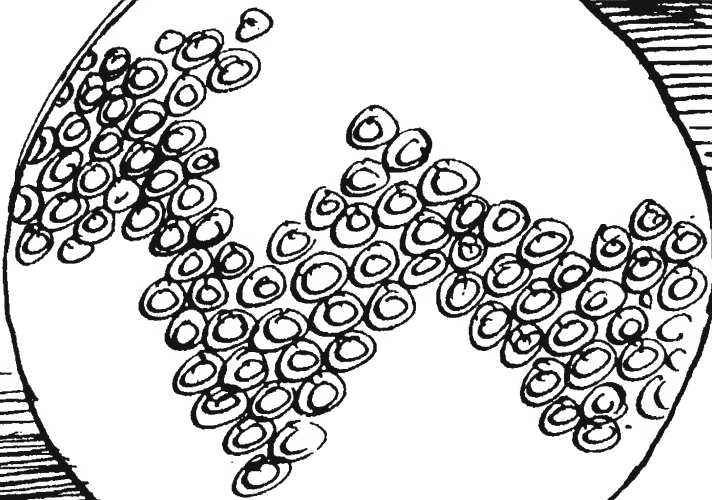
YES... LEEUWENHOEK HAS
ALREADY CORRUPTED
THE MORALS OF
THE FLEA...



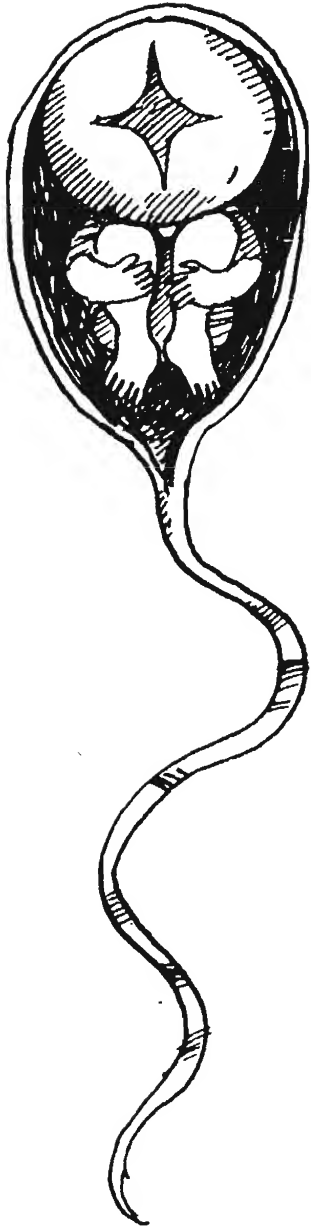


THE DUTCH SCIENTIST
MADE TWO MORE
GREAT DISCOVERIES:

HE WAS THE FIRST
TO SEE
BACTERIA,
THE ULTRA-SMALL
ORGANISMS WHICH
HAVE BECOME
SO IMPORTANT IN
MODERN GENETICS
RESEARCH.

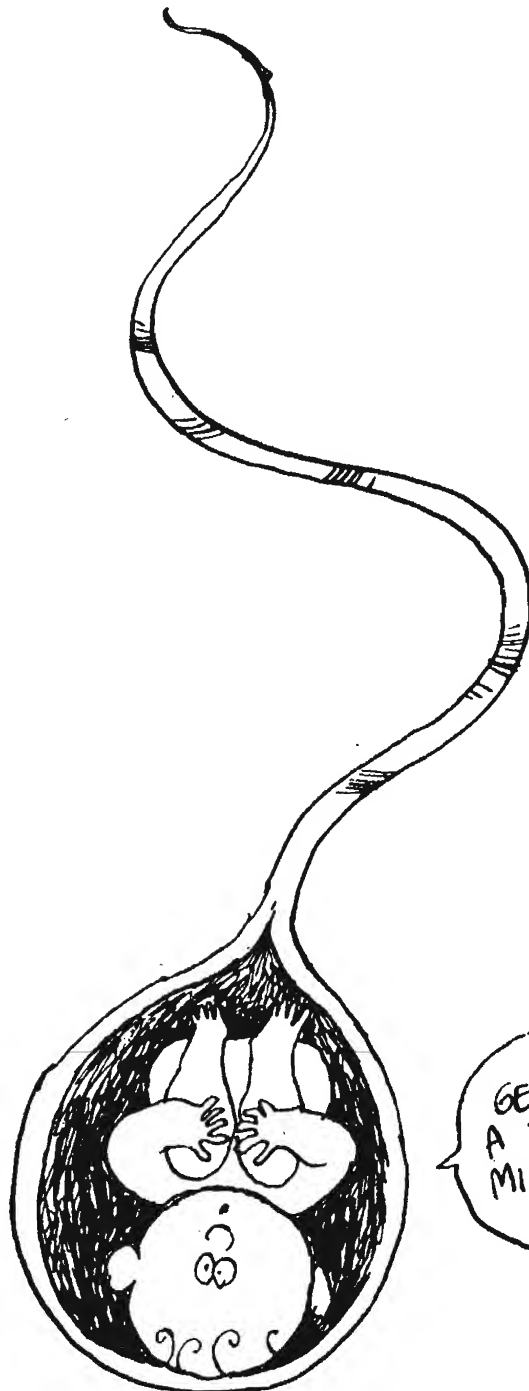


AND HE DISCOVERED
THE EXISTENCE OF
SPERM CELLS.
EXAMINING SEMEN,
LEEUVENHOEK SAW
MILLIONS OF THESE
TINY "WORMS."



ONE MIGHT SAY THAT THIS DISCOVERY OPENED A WHOLE CAN OF WORMS...OR THAT IT SPAWNED WRONG IDEAS... FOR INSTANCE, LEEUWENHOEK HIMSELF BELIEVED EACH SPERM CELL CONTAINED A COMPLETE NEW ORGANISM IN MINIATURE.

THE OBVIOUS PROBLEM WAS: IF THIS "PRE-FORMED" ORGANISM WAS A BOY, IT MUST ALREADY HAVE TINY TESTICLES, WHICH WOULD CONTAIN MINIATURE SPERM, WHICH WOULD EACH HAVE EVEN TINIER PREFORMED ORGANISMS... AD INFINITUM ET ABSURDUM !!!

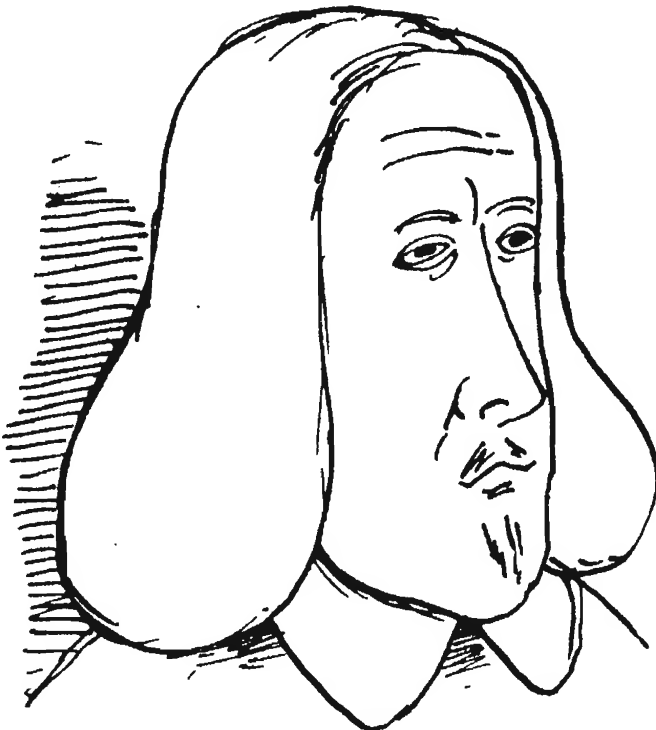
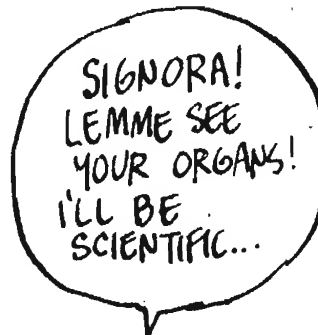


GET ME A TINY MICROSCOPE!!

EX OVO OMNIA

(AS LONG AS WE'RE TALKING LATIN!)

WHILE
LEEUVENHOEK
SPECULATED
ABOUT SPERM,
OTHER SCIENTISTS
WERE LOOKING
INTO THE
FEMALE
ROLE IN
REPRODUCTION...



WILLIAM HARVEY
(1578-1657) STUDIED
THE DEVELOPMENT
OF THE CHICK EMBRYO
AND CONVINCED
HIMSELF THAT ALL
ANIMALS MUST COME
FROM EGGS. "EX
OVO OMNIA," HE SAID:
"OUT OF EGG, ALL."

HARVEY BEGAN THE HUNT FOR THE MAMMALIAN EGG.

HE PERSUADED THE KING TO LET HIM LOOK FOR MAMMAL EGGS IN THE ROYAL DEER PARK... DOZENS OF DISSECTED DEER LATER, HARVEY HAD TO ADMIT FAILURE.

SIGH:
GUESS I' LAID
AN EGG...



EX OVO
OMELET!



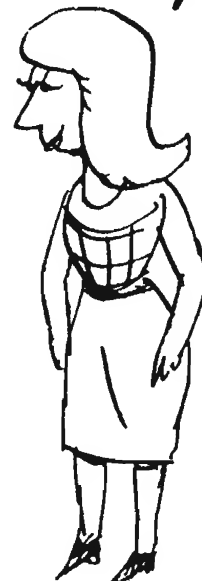
FOR 200 YEARS THE HUNT WENT ON... AND STILL NO ONE COULD LOCATE THE ELUSIVE EGG.

IT'S NOT HARD TO SEE WHY NOT... NOT ONLY IS THE MAMMALIAN EGG, MICROSCOPIC, IT'S ALSO FAIRLY RARE...



MAMMALS "LAY"
VERY FEW EGGS:
A HUMAN FEMALE
PRODUCES ONLY
ONE A MONTH,
IN CONTRAST
TO THE MALE
AND HIS
TENS OF MILLIONS
OF SPERM
CELLS.

WASTREL!



BUT THE SEARCH WENT ON...THERE WERE SOLID REASONS FOR BELIEVING MAMMALS HAD EGGS: WE HAVE OVARIES AND OVIDUCTS... IT WOULD BE PRETTY SILLY NOT TO HAVE EGGS, TOO...

YES,
PEOPLE ARE
JUST HIGHLY
EVOLVED
CHICKENS!



IN FACT, SCIENTISTS GREW SO SURE EGGS WERE THERE, THAT WHEN ONE WAS FINALLY SEEN—A DOG'S EGG, IN 1827—IT CAME AS MORE OF A RELIEF THAN A SURPRISE!!

HEY! DOGS
GOT EGGS!

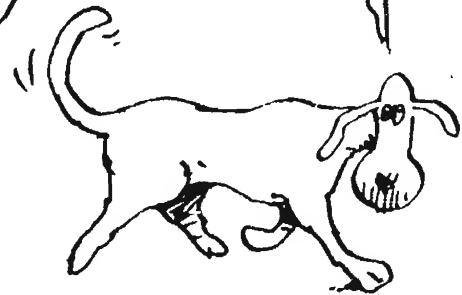
YOO-HOO!

OVER
HERE!

I SAW
IT!

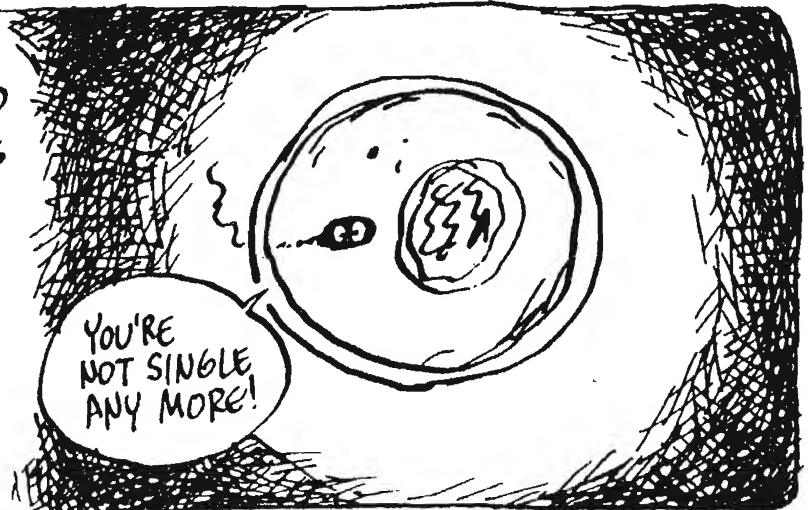
HEY!

SIGH:
IT'S ABOUT
TIME...



THE ONLY REMAINING RIDDLE WAS ANSWERED WHEN OSCAR HERTWIG OBSERVED THAT FERTILIZATION WAS THE UNION OF A SINGLE SPERM WITH A SINGLE EGG.

YOU'RE
NOT SINGLE
ANY MORE!



MEANWHILE,

SOME PROGRESS
HAD BEEN
MADE IN THE
QUESTION OF
PLANT SEX.

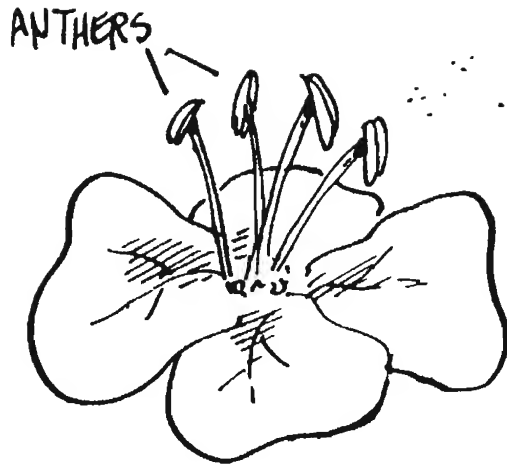


By 1700, THE
SEXUAL NATURE OF
PLANTS HAD BEEN
LARGELY RESOLVED
BY CAMERARIUS
(1665-1721), WHOSE
NAME EVEN SOUNDS
LIKE A PLANT...

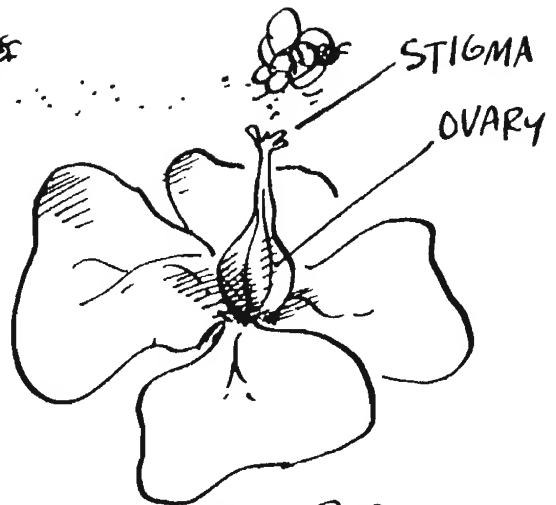
CAMERARIUS SHOWED THAT FLOWERS BORE SEX ORGANS
QUITE LIKE THOSE OF ANIMALS.

AND THEY STICK
THEM RIGHT IN
THE AIR...
SHAMEFUL!



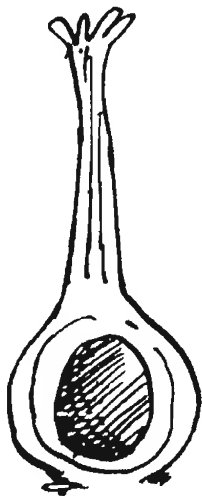


THE MALE PARTS, **ANTHERS**, CONTAIN POLLEN, WHICH IS LIKE SPERM IN ANIMALS.

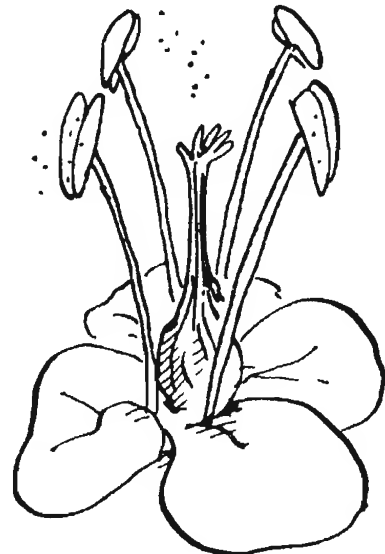


THE FEMALE PART IS THE **STIGMA**, TO WHICH THE POLLEN ATTACHES.

THE POLLEN (OR PART OF IT) THEN PENETRATES TO THE OVARY, CAUSING SEEDS TO DEVELOP



JUST TO COMPLICATE MATTERS, MANY FLOWERS HAVE BOTH MALE AND FEMALE ORGANS — AND SO THEY CAN FERTILIZE THEMSELVES.



SO BY THE EARLY 1800'S, BOTH PLANTS AND ANIMALS WERE KNOWN TO BE SEXUAL... THE MALE CONTRIBUTED POLLEN OR SPERM; THE FEMALE EGGS... AND SPONTANEOUS GENERATION WAS ON ITS LAST LEGS — ALMOST...

MY MOTHER SAID BABIES COME FROM CABBAGE LEAVES...

ARE YOU CALLING MY MOTHER A LIAR ??



TO BREED OR NOT TO BREED?



WITH ALL
THIS TALK
ABOUT SCIENTISTS,
LET US NOT
FORGET
THE PRACTICAL
GENETICISTS -

NAMELY, THE
FARMERS AND
STOCKBREEDERS
WHO DID ALL
THE DIRTY
WORK OUT
IN THE
FIELDS.

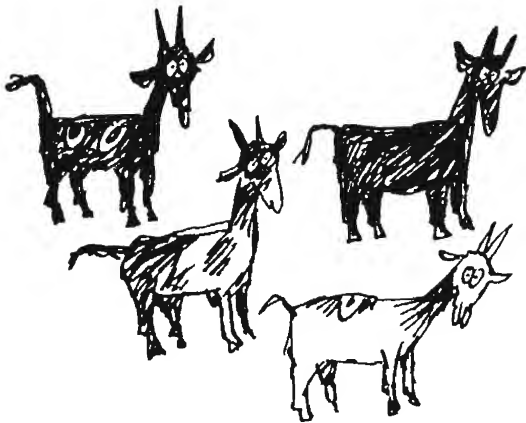


FOR THEM, THE
EARLY 19TH CENTURY
WAS ALSO A
TIME OF GREAT
PROGRESS WHEN
PRACTICAL
QUESTIONS OF
FARMING WOULD
LEAD, MORE OR
LESS DIRECTLY,
TO THE
DISCOVERY OF
THE GENE.

LET'S SEE WHAT THEY ALREADY KNEW FROM EXPERIENCE:

1.

SOME STABLE VARIETIES NEARLY ALWAYS BREED TRUE, THEIR OFFSPRING HAVING THE SAME CHARACTERISTICS AS THEIR PARENTS. SOME COMMON EXAMPLES ARE MACKINTOSH APPLES, ARABIAN HORSES, LABRADOR RETRIEVERS, PEOPLE WITH BLUE EYES, ETC ETC ETC...



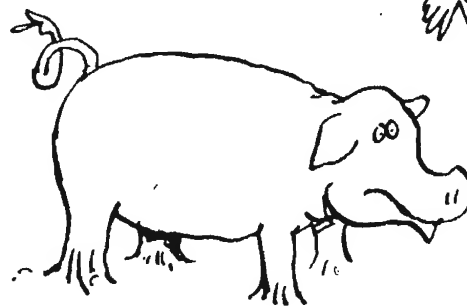
ON THE OTHER HAND, SOME BREEDING GROUPS SHOW GREAT VARIATION. JACOB'S FLOCK IS AN EXAMPLE OF VARIABLE COLOR. PEOPLE WITH BROWN EYES CAN HAVE BLUE-EYED CHILDREN.

2.

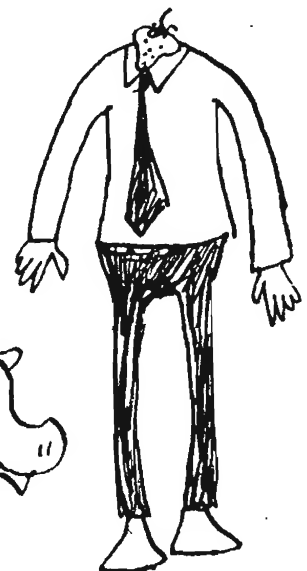
IT IS SOMETIMES POSSIBLE TO MATE PARENTS FROM TWO DIFFERENT VARIETIES TO FORM **HYBRIDS.**

FOR EXAMPLE, A MULE IS HALF HORSE AND HALF DONKEY. OF COURSE, NOT ALL HYBRIDS ARE POSSIBLE !!!

IMPOSSIBLE HYBRIDS:



PIG/TREE



HUMAN/STRAWBERRY

HYBRIDS ARE DIFFICULT TO PREDICT... THEY MAY SEEM VIRTUALLY IDENTICAL TO ONE PARENT OR THEY MAY COMBINE FEATURES OF BOTH — AND WHEN HYBRIDS BREED WITH HYBRIDS, THE RESULT IS VARIATION IN THE EXTREME !!

HARD TO BELIEVE YOU'RE MY BROTHER!

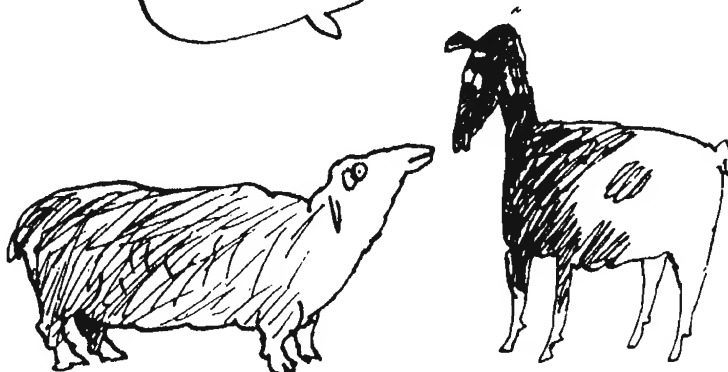


3. ALL VARIETIES, EVEN STABLE ONES, OCCASIONALLY PRODUCE "SPORTS" — OFFSPRING DIFFERENT FROM EITHER PARENT. THESE ARE OFTEN GROSSLY DEFECTIVE "MONSTROSITIES"...

OUR CHILD IS A MESS!

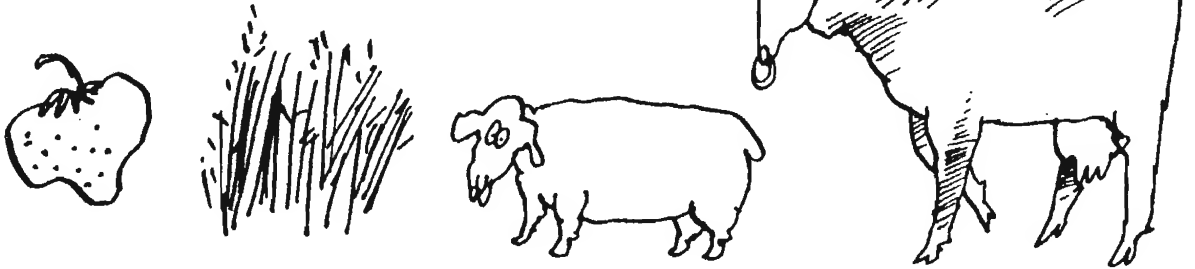


A DACHSHEEP!



BUT SOMETIMES THE SPORT DIFFERS ONLY SLIGHTLY, LIKE THE STUBBY-LEGGED SHEEP WHICH APPEARED AROUND 1800.

BY CROSSING THESE SPORTS BACK WITH NORMAL TYPES, 19TH-CENTURY FARMERS HAD MANAGED TO CREATE SEVERAL NEW STABLE VARIETIES. THERE WERE NEW TYPES OF WHEAT, PEAS, AND STRAWBERRIES, HORNLESS CATTLE, AND STUBBY-LEGGED SHEEP.



BUT IT WAS STILL A MATTER OF TRIAL AND ERROR... IT DIDN'T ALWAYS WORK... AND SO PEOPLE BEGAN TO WONDER IF THERE MIGHTN'T BE A SCIENTIFIC WAY OF SELECTING ADVANTAGEOUS TRAITS TO CREATE NEW VARIETIES.

IF WE COULD BREED A SIX-LEGGED HORSE, WE'D CLEAN UP IN GLUE!

AND A THREE-LEGGED HUMAN COULD PUT HIS FOOT IN HIS MOUTH AND STILL WALK!



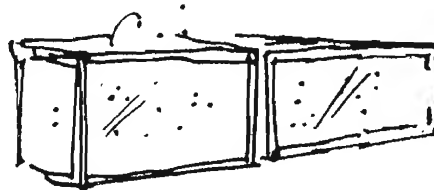
HOWEVER,

DESPITE A GOOD DEAL
OF WORK, NO TRULY GENERAL
LAWS OF INHERITANCE WERE
DISCOVERED.

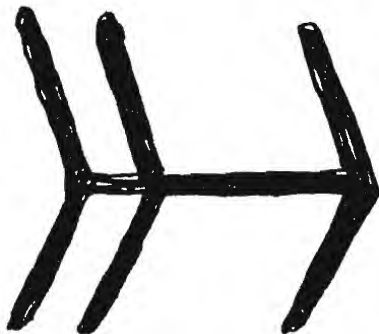
SOME INVESTIGATORS CONFUSED THEMSELVES BY CROSSING
BREEDS THAT DIFFERED IN TOO MANY CHARACTERISTICS...



OTHERS FAILED
TO KEEP A
CAREFUL COUNT
OF THE NUMBER
OF VARIETIES
PRODUCED
FROM EACH
CROSS.

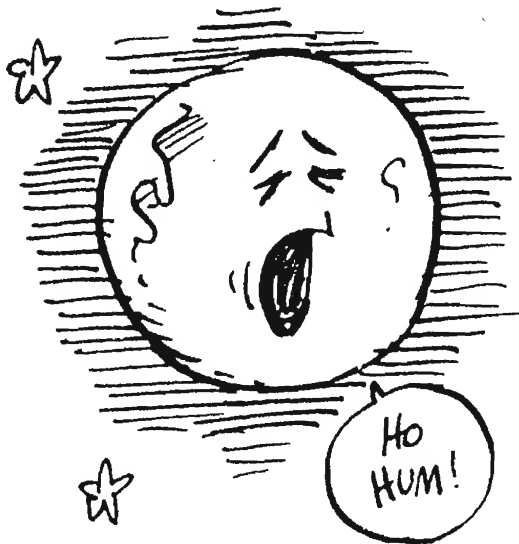


*O# FLEAS
ARE HARD TO
KEEP TRACK
OF!



INDEED, THE PROBLEM SEEMED
HOPELESS... GRADUALLY, SCIENTISTS
GAVE UP TRYING AND TURNED TO
EASIER PROBLEMS... AND THAT IS WHY,
WHEN THE LAWS OF INHERITANCE WERE
FINALLY FIGURED OUT, THE
DISCOVERY WAS IGNORED FOR
THIRTY YEARS...

MONK FINDS GENE; WORLD YAWNS!



FIFTY YEARS OF RESEARCH HAD FAILED TO FIND ANY PRECISE LAW OF INHERITANCE. OBVIOUSLY, DISCOVERING THE RIGHT FORMULA, IF POSSIBLE, WAS A JOB REQUIRING SUPERHUMAN PATIENCE, UNLIMITED TIME, AND, AS IT HAPPENED, A MIRACLE OF LUCK.

NO WONDER IT HAPPENED IN A MONASTERY...

GREGOR MENDEL

(1822 - 1884) WAS AN AUGUSTINIAN MONK FROM BRÜNN, AUSTRIA. IN HIS SPARE TIME, MENDEL BRED PEA PLANTS IN THE MONASTERY GARDENS.

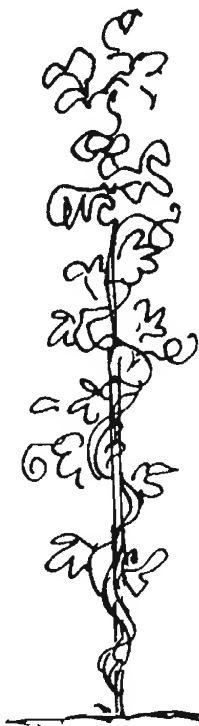


BUT MENDEL WAS NOT JUST AN AMATEUR GARDENER, BUT A **SCIENTIST** WHO STUDIED HIS PEA PLANTS MOST CAREFULLY — HE CALLED THEM HIS "CHILDREN."

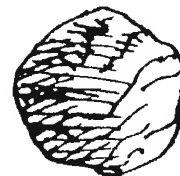
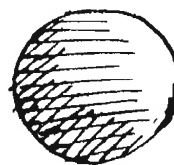


WHAT KIND OF DAD DOES EXPERIMENTS ON HIS KIDS?

CHOOSING PEAS WAS THE MIRACLE OF LUCK: THEY ARE PERFECTLY SUITED TO GENETIC RESEARCH, WITH A NUMBER OF STABLE VARIETIES WHICH MAY FORM HYBRIDS:



THERE WAS A TALL VARIETY AND A SHORT ONE...



ONE TYPE MADE SMOOTH, ROUND PEAS, WHILE ANOTHER'S WERE LUMPY AND WRINKLED...



SOME PODS WERE PLUMP, WHILE OTHERS WERE PINCHED...

THERE WERE GREEN PEAS AND YELLOW; GREY SEED-COATS AND WHITE; WHITE FLOWERS AND PURPLE. THERE WERE DIFFERENCES IN THE COLOR OF THE UNRIPE PODS, THE COLOR OF SEED ALBUMIN, AND THE POSITION OF THE FLOWERS.

EVERY PEA FLOWER
HAS BOTH MALE
AND FEMALE
ORGANS, SO THEY
ORDINARILY
FERTILIZE
THEMSELVES.

UNLESS
WE PRACTICE
: AHEM :
FAMILY PLANNING!

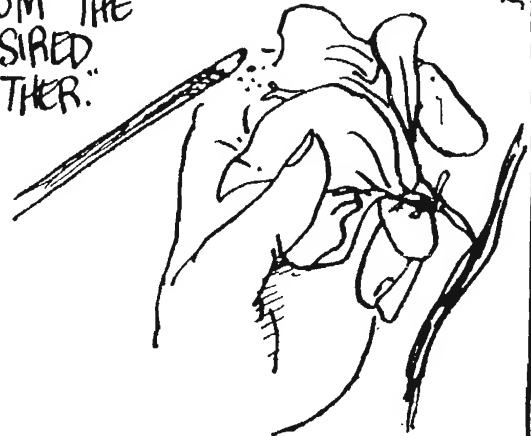


HOW MENDEL MADE HYBRIDS:

FIRST HE SNIPPED
OFF THE ANTHERS
WHILE STILL IMMATURE
TO PREVENT
"SELFING."



THEN HE DUSTED THE
STIGMA WITH
POLLEN TAKEN
FROM THE
DESIRED
"FATHER."



FINALLY, HE TIED BAGS
OVER THE FLOWERS
TO KEEP OUT ANY
STRAY
POLLEN.

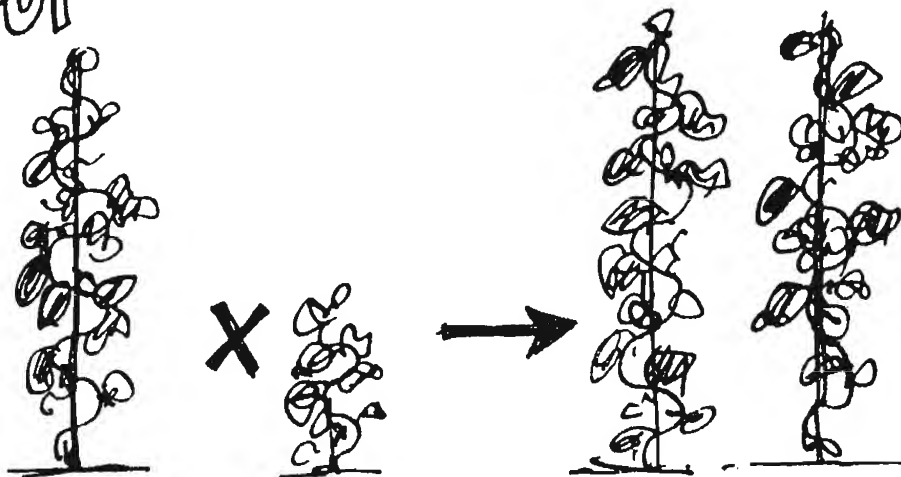


IN THIS
WAY
MENDEL
WAS
ABLE TO
CONTROL
THE
PARENTAGE
OF EACH
GENERATION.

PSST!
I THINK
THE MONK
IS PLAYING
GOD!!



MENDEL'S FIRST MAJOR RESULT WAS THE DISCOVERY OF **DOMINANCE**. WHAT HAPPENED WHEN A TALL PLANT WAS CROSSED WITH A SHORT? ONE MIGHT EXPECT MEDIUM-SIZED PLANTS, **BUT**



IN FACT,
ALL THE
HYBRIDS
WERE
TALL !!

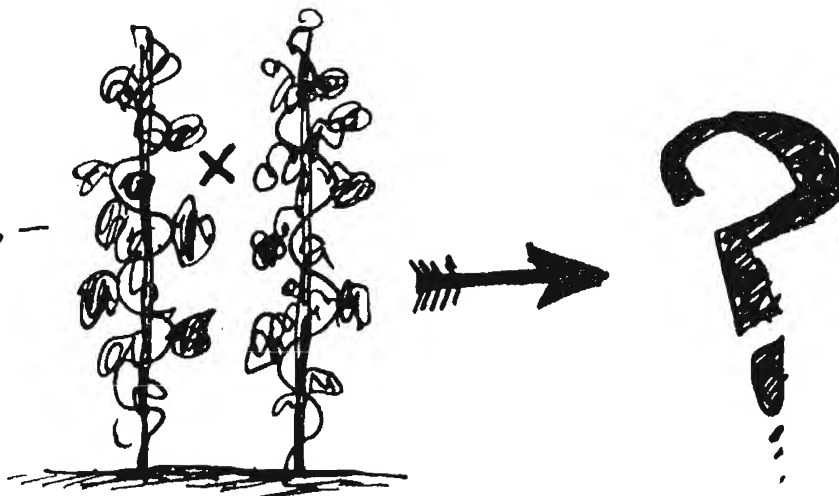
MENDEL EXPRESSED THIS BY SAYING THAT TALLNESS WAS **DOMINANT** OVER SHORTNESS (IN PEAS!). THE TRAIT OF SHORTNESS IS THEN CALLED **RECESSIVE**. IN EVERY CASE, ONE TRAIT WAS FOUND TO BE **DOMINANT**.



ROUND SEEDS ARE
DOMINANT OVER WRINKLED;
PLUMP PODS OVER
PINCHED; GREY SEED-
COATS OVER WHITE
SEED-COATS, ETC
ETC ETC...

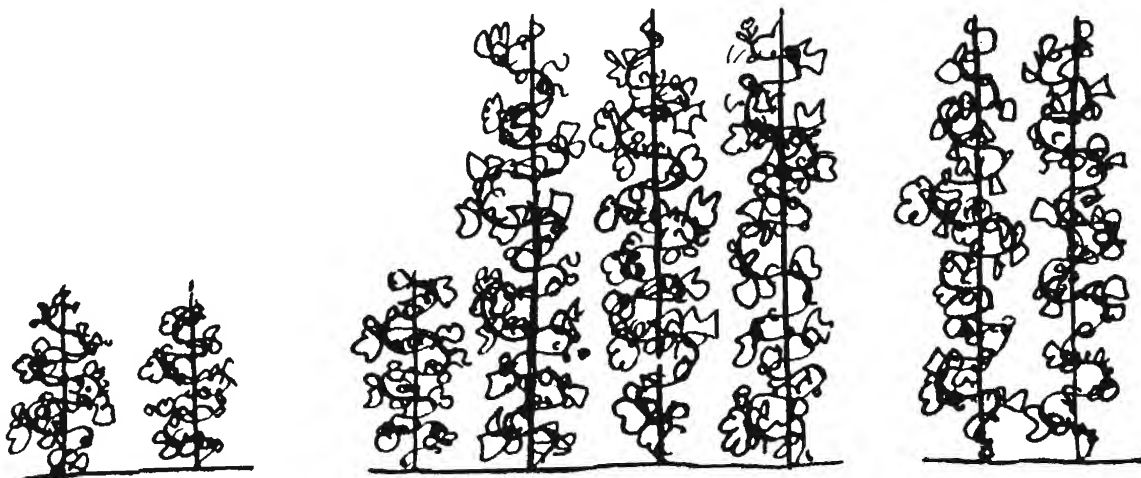
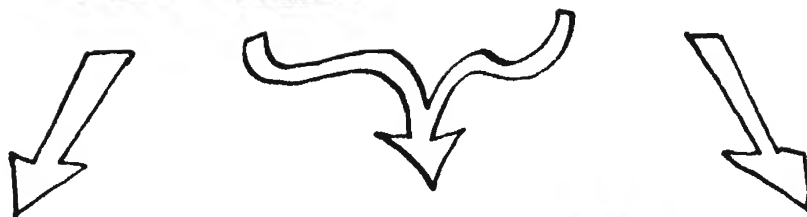
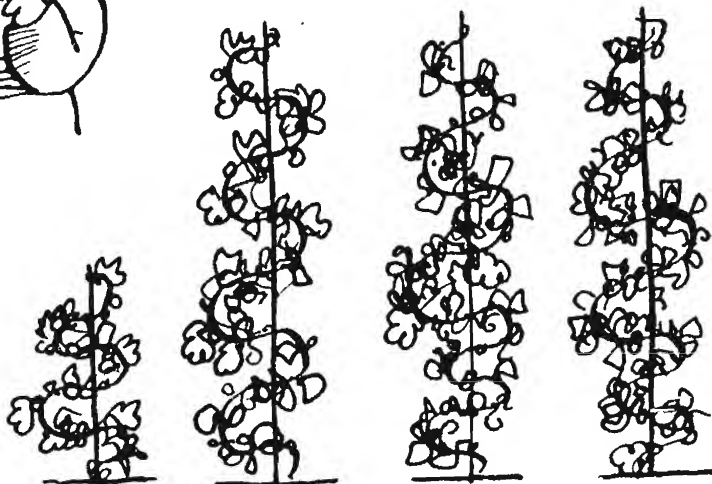
IT DIDN'T MATTER WHICH PARENT CONTRIBUTED THE POLLEN AND WHICH THE EGG. A TALL-SHORT HYBRID WAS ALWAYS TALL.

THE FUN
BEGINS WHEN
YOU START
BREEDING
THE HYBRIDS -



WHEN THE HYBRIDS
SELF-FERTILIZED, ABOUT
 $\frac{1}{4}$ OF THEIR OFFSPRING
WERE SHORT.

THE RECESSIVE
TRAIT REAPPEARED!!



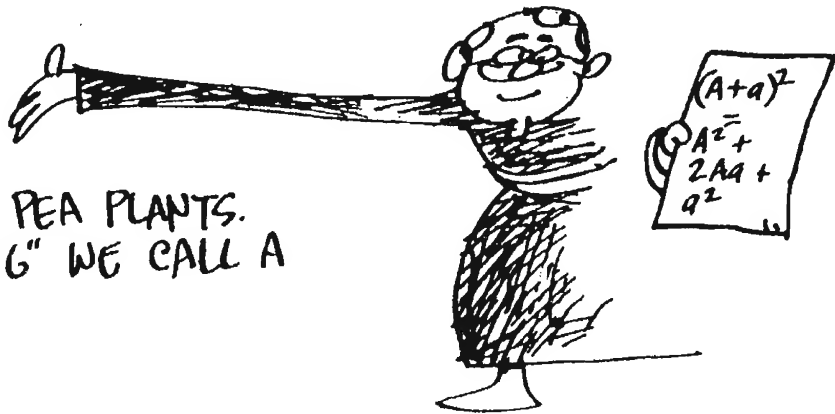
CONTINUING THE
SELF-FERTILIZATION,
MENDEL FOUND THAT
ABOUT ONE TALL IN
THREE PRODUCED
ONLY TALLS, WHILE
THE OTHERS YIELDED
BOTH TALLS AND
SHORTS IN THE
RATIO 3:1.
THE SHORTS BRED
ONLY SHORTS.

MENDEL'S INTERPRETATION:

THERE IS SOMETHING IN POLLEN AND EGG WHICH DETERMINES THE HEIGHT OF PEA PLANTS. THIS "SOMETHING" WE CALL A

GENE.

IT'S MATHEMATICAL!



EACH POLLEN GRAIN AND EGG HAS ONE HEIGHT GENE, SO THE PLANT FORMED BY THEIR UNION HAS TWO.

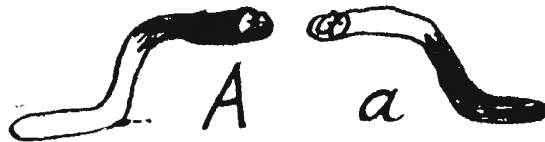
THE GENE MAY BE ONE OF TWO DISTINCT TYPES, OR

ALLELES.

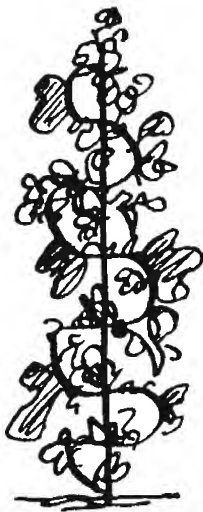
ONE ALLELE, A, IS FOR TALLNESS; THE OTHER ONE, a, IS FOR SHORTNESS.

GENES MAKE SHORTS?

CUT-OFFS...



A PLANT MAY HAVE THE SAME OR DIFFERENT ALLELES.



AA



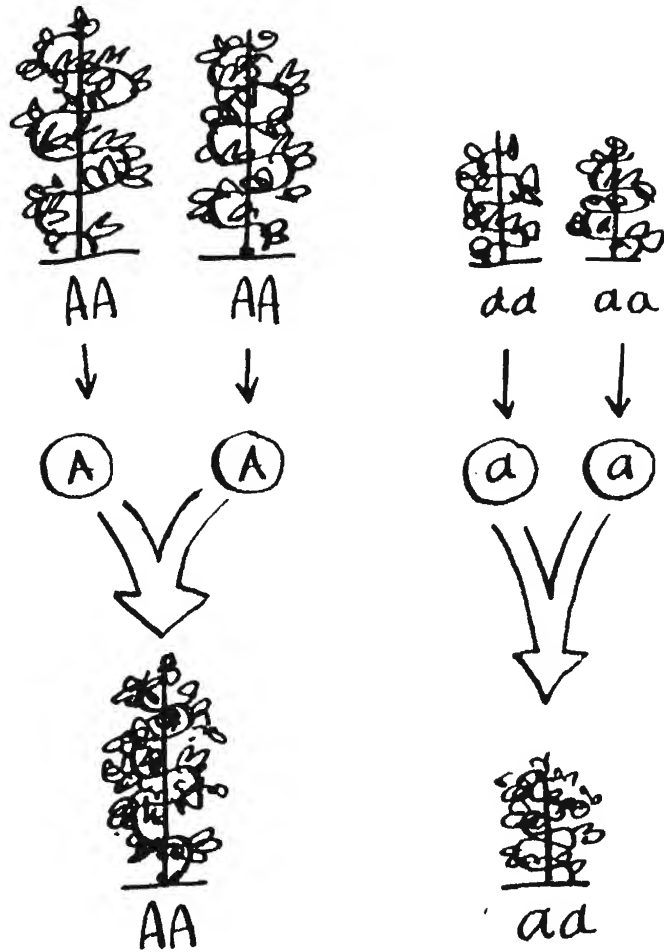
aa



Aa

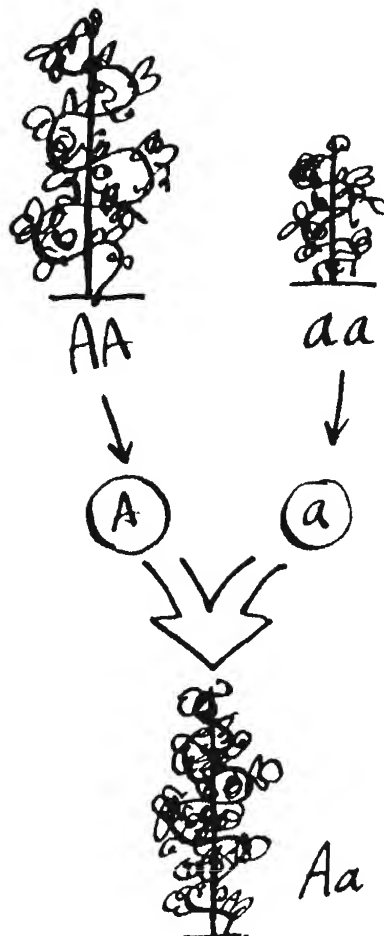
THE ALLELE A IS DOMINANT OVER a. THAT IS, THE PLANT WITH THE COMBINATION Aa IS TALL. THE ALLELES DO NOT "BLEND."

WHAT HAPPENS
WHEN AA
BREEDS WITH
AA ? POLLEN AND
EGG EACH GET
ONE COPY OF
THE GENE...
IN THIS CASE,
THE ALLELES
ARE THE SAME -
A - SO THE
OFFSPRING WILL
AGAIN BE AA, OR
TALL. LIKEWISE,
aa CAN YIELD
ONLY aa. THESE
ARE THE STABLE
SHORT & TALL
VARIETIES.

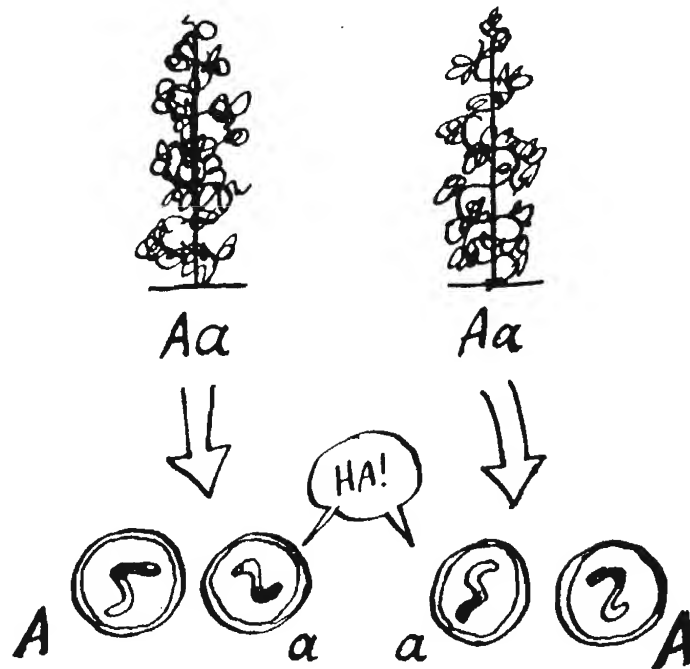


MENDEL'S FIRST
HYBRID WAS A
CROSS BETWEEN
AA AND aa:
THE POLLEN (OR EGG)
FROM AA CONTAINS
ONLY A, WHILE
THE EGG (OR POLLEN)
FROM aa CONTAINS
ONLY a.

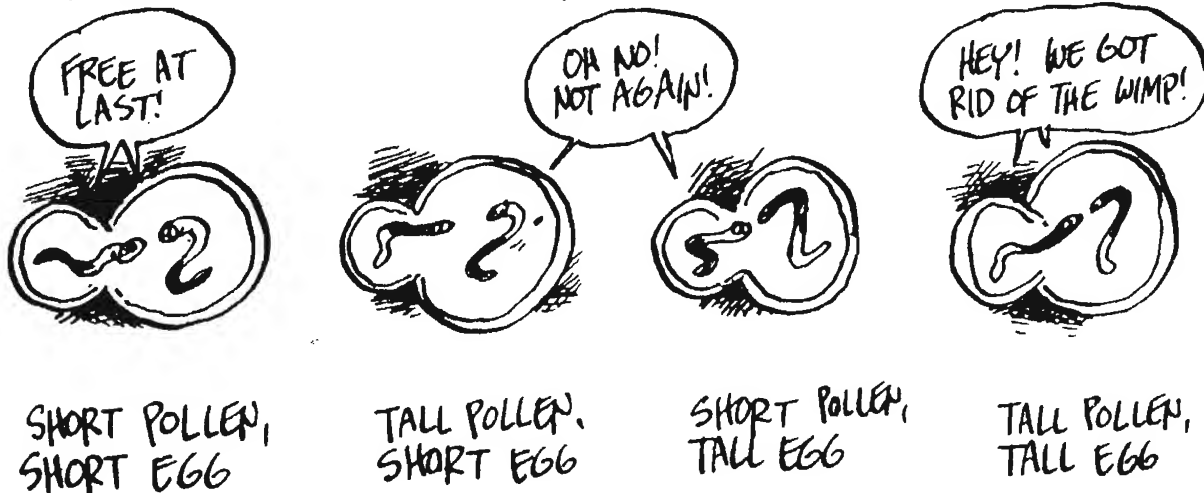
RESULT:
Aa, WHICH
IS TALL.



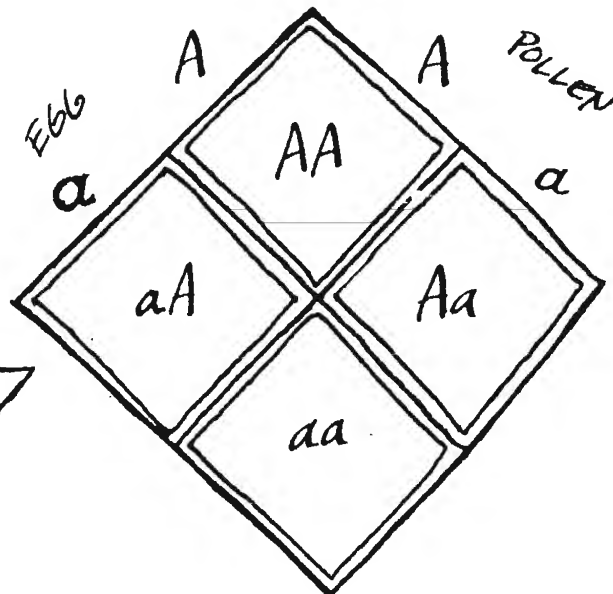
WHEN THE HYBRID
SELF-FERTILIZES,
ITS ALLELES
A AND a ARE SORTED
OUT RANDOMLY
AMONG THE POLLEN
GRAINS AND EGGS.
BOTH A AND a
APPEAR, AND IN
ROUGHLY EQUAL
PROPORTIONS.



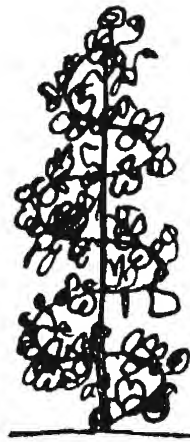
WHEN EGGS AND POLLEN UNITE, THERE ARE FOUR POSSIBILITIES:



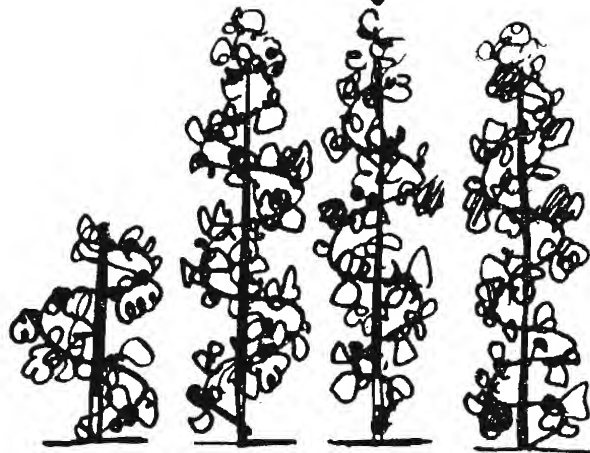
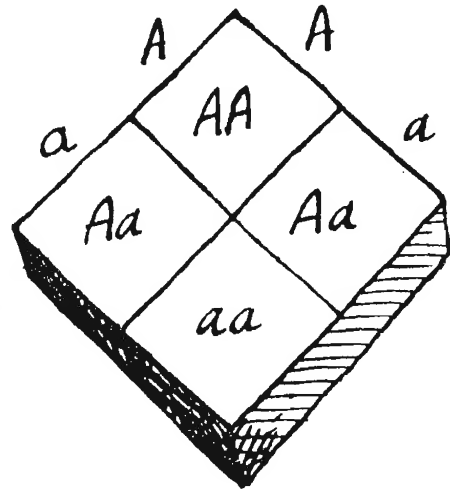
WHICH ARE
SUMMARIZED IN
THIS SQUARE:
EACH POSSIBLE
OFFSPRING
APPEARS IN ONE
OF THE
SMALL
BOXES.



HERE AGAIN ARE THE
HYBRID'S DESCENDANTS,
AS MENDEL OBSERVED
THEM. THE FIRST
GENERATION AGREES
WITH THE CROSSING
SQUARE:



Aa



aa

Aa

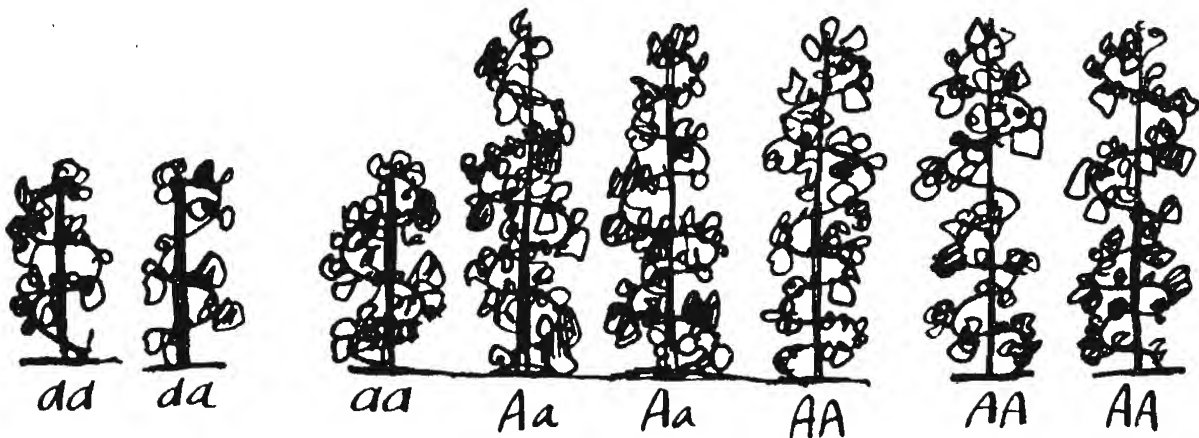
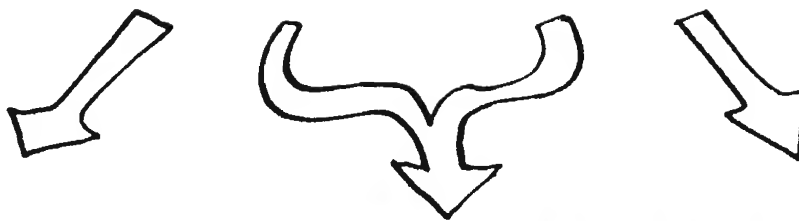
aA

AA

$\frac{1}{4}$ TRUE-BREEDING
TALLS (AA)

$\frac{1}{2}$ TALLS WHICH
MAY BREED
SHORTS (Aa)

$\frac{1}{4}$ TRUE-BREEDING
SHORTS (aa)



aa

aa

aa

Aa

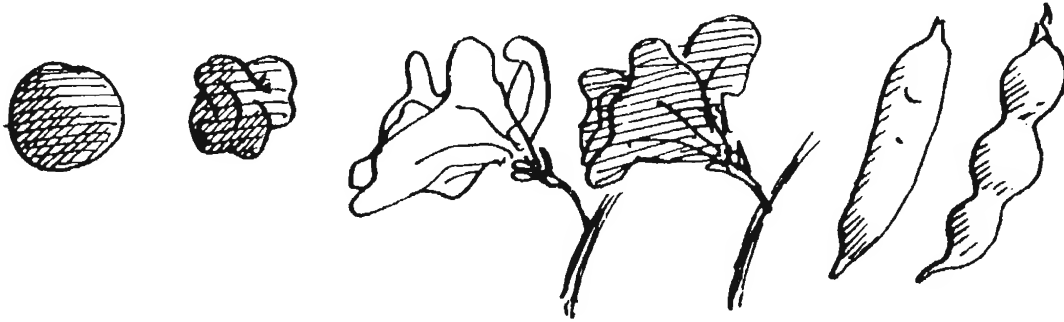
Aa

AA

AA

AA

MENDEL ALSO CROSSED SMOOTH-PEA PLANTS WITH WRINKLED, PURPLE FLOWERS WITH WHITE, ETC ETC ETC. IN EVERY CASE, HE FOUND THE CHARACTERISTIC TO BE CONTROLLED BY A SINGLE GENE WITH TWO DIFFERENT ALLELES, ONE OF WHICH WAS DOMINANT OVER THE OTHER.



SO IT SEEMED THAT POLLEN AND EGG WERE BOTH FULL OF THESE LITTLE "SOMETHINGS," ONE FOR EVERY HEREDITARY TRAIT OF THE ORGANISM. PRETTY CROWDED!



HOW CAN I DO MY JOB IN THIS MOB?

YOU DON'T HAVE TO: YOU'RE RECESSIVE!



LORD KNOWS THEY MUST BE TINY!!

WITHOUT EVER SEEING A GENE, MENDEL CONCLUDED THAT HEREDITY IS CONTROLLED BY THESE "ATOMS OF INHERITANCE," WHICH NEVER BREAK OR BLEND, MAINTAINING THEIR CHARACTER FROM GENERATION TO GENERATION.

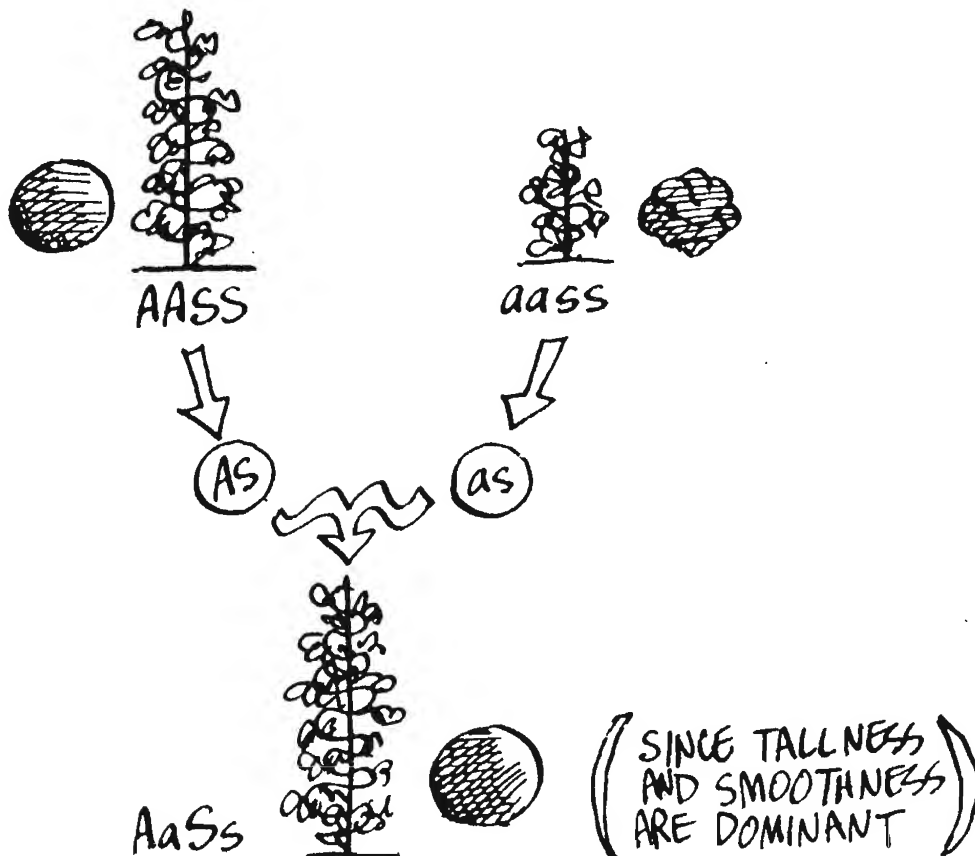
INITIALLY, MENDEL MADE CROSSES BETWEEN PLANTS DIFFERING IN TWO CHARACTERISTICS — FOR EXAMPLE, A TALL PLANT WITH SMOOTH SEEDS AND A SHORT PLANT WITH WRINKLED SEEDS. THE QUESTION HERE IS: ARE HEIGHT AND SMOOTHNESS CORRELATED SOMEHOW, OR DO THEY ACT INDEPENDENTLY WHEN THE PLANT REPRODUCES??



CALL THE ALLELE FOR SMOOTH SEEDS S AND THAT FOR WRINKLED SEEDS s . S IS DOMINANT, SO



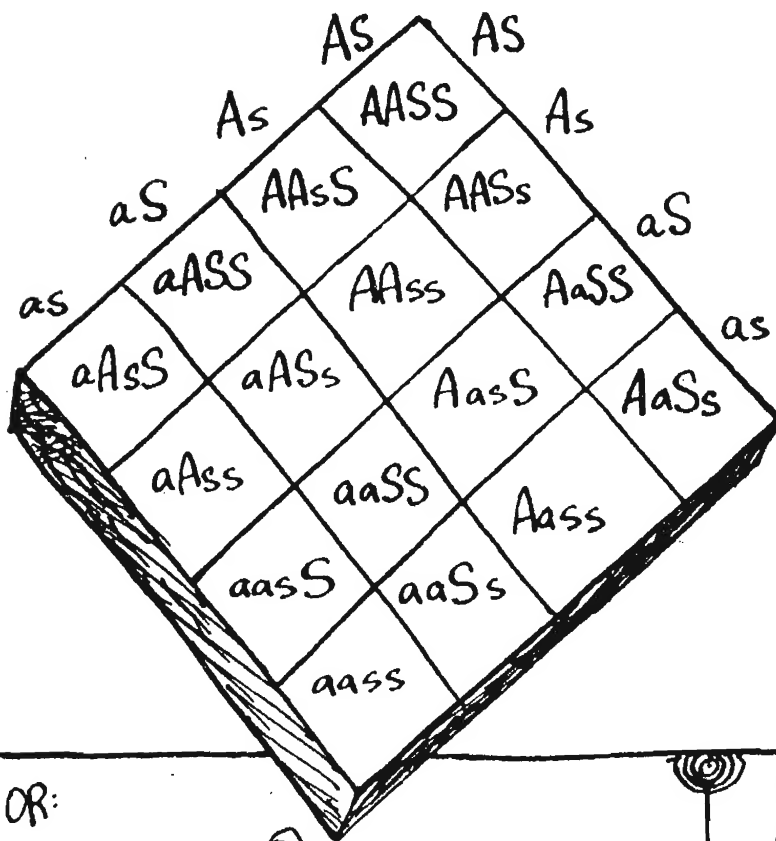
THE CROSS IS BETWEEN $AASS$ AND $aass$.



NOW FOR THE SELF-POLLINATION OF THE HYBRID:



THE GENES FOR HEIGHT AND SMOOTHNESS SORT OUT INDEPENDENTLY OF EACH OTHER, THEN ALL THESE POSSIBLE POLLENS AND EGGS WOULD BE EQUALLY LIKELY:



IN WHICH CASE, THE CROSSING SQUARE LOOKS LIKE THIS.

OR:

- | | | |
|--------|---|-------------------|
| 1 AASS | } | 9 TALL, SMOOTH |
| 2 AASs | | |
| 2 AaSS | | |
| 4 AaSs | | |
| 1 AAss | } | 3 TALL, WRINKLED |
| 2 Aass | | |
| 1 aaSS | } | 3 SHORT, SMOOTH |
| 2 aaSs | | |
| 1 aass | | 1 SHORT, WRINKLED |

AND THIS IS WHAT MENDEL OBSERVED — A RATIO OF 9:3:3:1. THIS EXPERIMENT, AND OTHERS WITH DIFFERENT COMBINATIONS, PROVED THE **PRINCIPLE OF INDEPENDENT ASSORTMENT**: THE ALLELES OF ONE GENE SORT OUT INDEPENDENTLY OF THE ALLELES OF ANOTHER. (WE'LL SOON SEE THAT THIS 'PRINCIPLE' ISN'T QUITE TRUE!)

NOW THAT WE'VE SEEN
HOW GENES WORK,
HERE'S A BIT OF
GENETICS JARGON,
IN CASE YOU SHOULD
EVER WANT TO
EAVESDROP ON A
MODERN GENETICIST...



THIS GEN-TEK DEAL
MEANS ELEPHANT
BUCKS, BABY... WE'RE
TALKING RECOMBINANT
BANK ACCOUNTS,
PROFESSOR...

WELL... NOT THAT KIND
OF JARGON...

GENETICISTS DISTINGUISH
BETWEEN AN ORGANISM'S
PHENOTYPE - WHAT IT
LOOKS LIKE - AND ITS
GENOTYPE - WHAT
ALLELES IT HAS.



AA



Aa

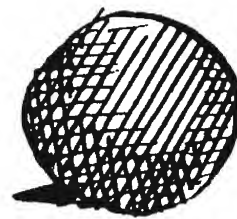
SAME
PHENOTYPE,
DIFFERENT
GENOTYPE

AN ORGANISM IS
HOMOZYGOUS WITH
RESPECT TO A
GIVEN GENE IF ITS
TWO ALLELES ARE
THE SAME, AND
HETEROZYGOUS
IF THEY'RE
DIFFERENT.



SS

HOMOZYGOUS



Ss

HETEROZYGOUS

SO NOW YOU KNOW
WHAT A GENETICIST
MEANS BY
"PHENOTYPICALLY SMOOTH,
GENOTYPICALLY
HETEROZYGOUS."



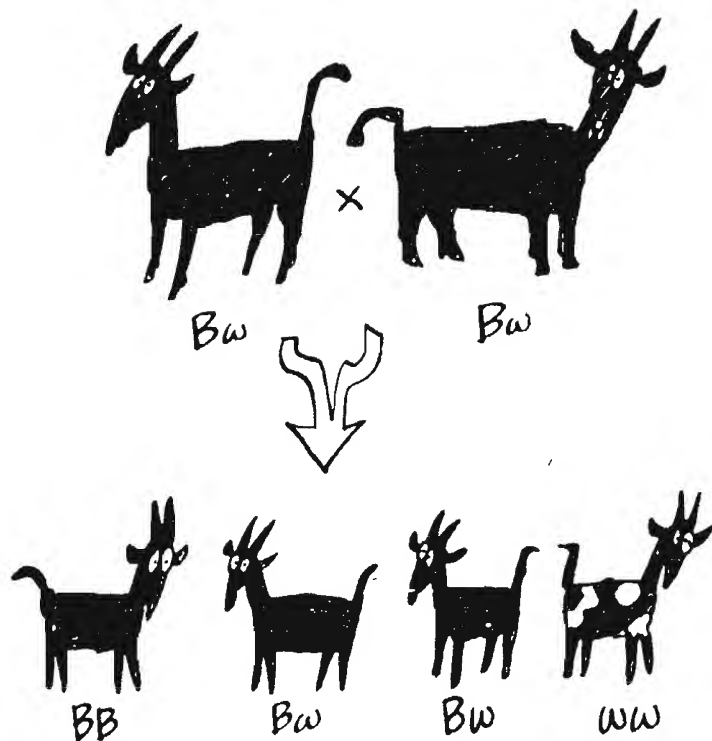
YES...
NOW TELL
ME ABOUT
RECOMBINANT
BANK
ACCOUNTS...

INCIDENTALLY — WE'RE NOW IN A POSITION TO UNDERSTAND JACOB'S SPECKLED FLOCK:



SPELL IT OUT FOR ME!

THE ALLELE FOR A BLACK COAT, CALL IT B , WAS DOMINANT. THERE WAS ALSO A RECESSIVE ALLELE, w , FOR WHITE SPECKLES. MANY OF LABAN'S PHENOTYPICALLY BLACK ANIMALS SECRETLY HARBORED THIS w , SO THEIR KIDS WERE SOMETIMES SPECKLED.*



IN OTHER WORDS —

THOSE GOATS WERE HETEROZY- GOATS!



* ACTUALLY, THE GENETICS OF COAT COLOR ARE MORE COMPLEX, BUT THE PRINCIPLE IS THE SAME: RECESSIVE ALLELES.

QUESTION:

IF YOU SEE A DOMINANT PHENOTYPE, HOW CAN YOU TELL IF IT'S A HETEROZYGOTE?

IS IT POLITE TO ASK?



FOR INSTANCE, IN HUMANS BROWN EYES ARE DOMINANT OVER BLUE. CALL THE GENES B AND b , RESPECTIVELY.



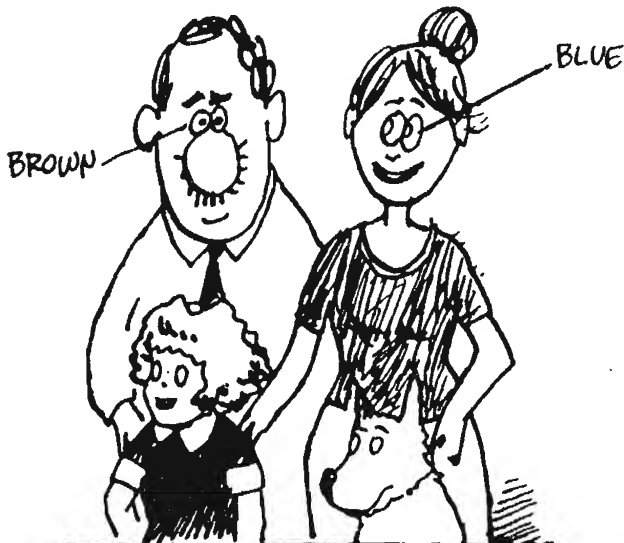
HOW CAN WE TELL IF THIS BROWN-EYED PERSON IS BB OR Bb ?

ONE WAY IS TO CROSS HIM WITH A RECESSIVE HOMOZYGOTE— I.E., A BLUE-EYED PERSON, bb .



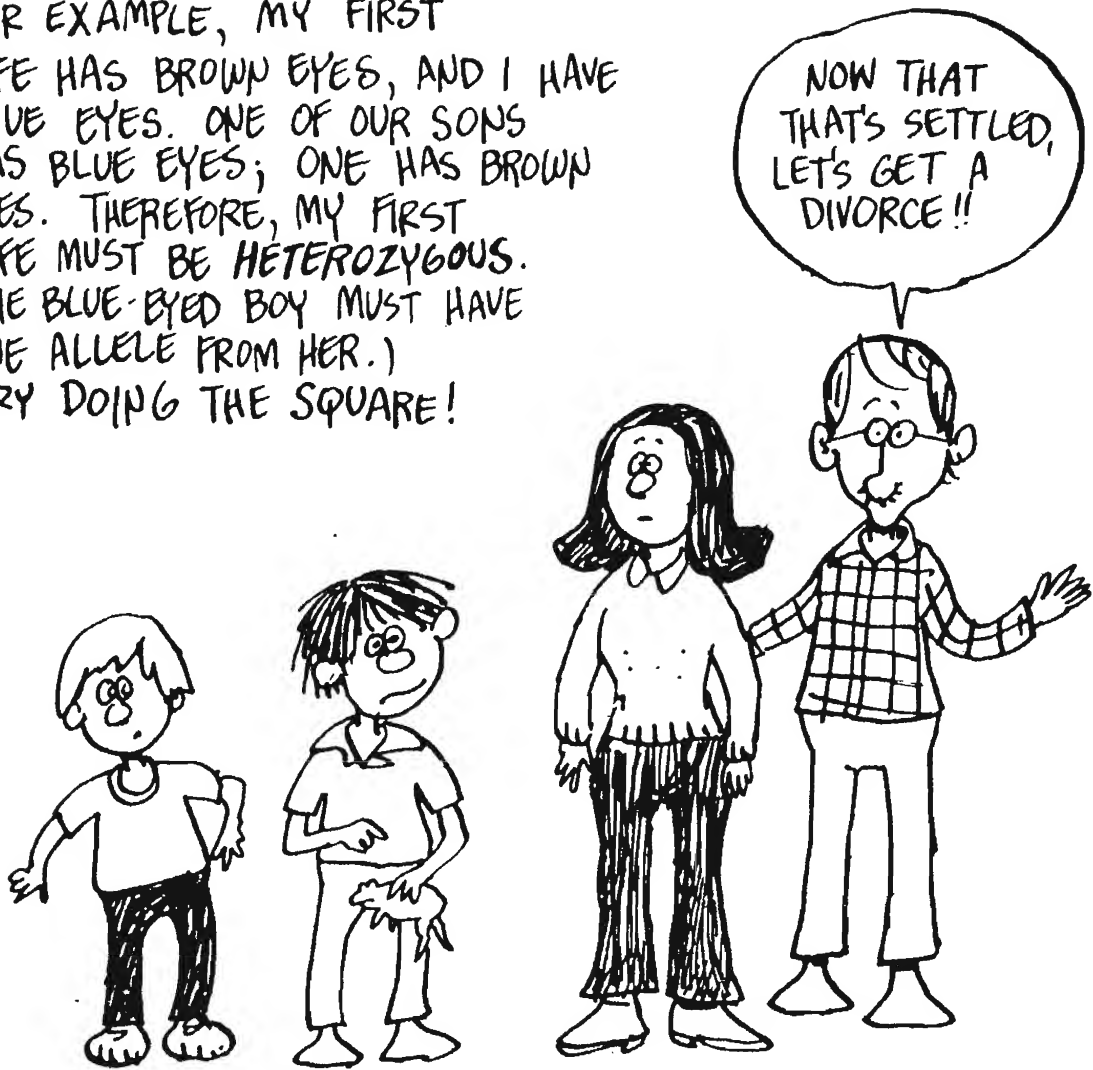
SORRY... I HAVE TO BACK OUT OF THIS EXPERIMENT... MONK'S VOWS, YOU KNOW...

O.K... WE'LL USE SOMEBODY ELSE...



IF ANY OF THE LITTLE HYBRIDS HAS BLUE EYES, THE BROWN-EYED PARENT MUST HAVE BEEN A **HETEROZYGOTE**, Bb . IF HE HAD BEEN BB , ALL THE CHILDREN WOULD HAVE BEEN Bb , WITH BROWN EYES.

FOR EXAMPLE, MY FIRST WIFE HAS BROWN EYES, AND I HAVE BLUE EYES. ONE OF OUR SONS HAS BLUE EYES; ONE HAS BROWN EYES. THEREFORE, MY FIRST WIFE MUST BE HETEROZYGOUS. (THE BLUE-EYED BOY MUST HAVE ONE ALLELE FROM HER.) TRY DOING THE SQUARE!



MY SECOND WIFE HAS BLUE EYES LIKE ME. IF OUR CHILD HAD BROWN EYES, WHAT WOULD WE MAKE OF THAT? BETTER ASK THE MILKMAN!!



SOME EXAMPLES
OF DOMINANT AND
RECESSIVE GENES
IN HUMANS:



★ BROWN EYES ARE
DOMINANT OVER BLUE
EYES.

★ COLOR VISION IS
DOMINANT OVER COLOR
BLINDNESS.

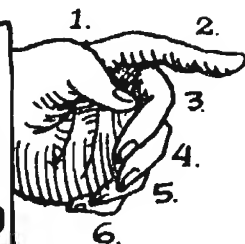
★ HAIRY HEADS ARE
DOMINANT OVER BALD
ONES.

★ THE ABILITY TO CURL
THE TONGUE IS DOMINANT
OVER THE INABILITY TO
CURL THE TONGUE.

★ EXTRA FINGERS ARE
DOMINANT OVER FIVE
FINGERS (ODD BUT TRUE!).

A DOUBLE DOSE OF RECESSIVES
ALSO CAUSE SUCH
RARE DISEASES AS HEMO-
PHILIA, SICKLE-CELL ANEMIA,
TAY-SACHS SYNDROME,
THALASSEMIA, DWARFISM...

TO SUM
UP...





MY PRINCIPAL RESULTS:

1 HEREDITARY TRAITS ARE GOVERNED BY GENES WHICH RETAIN THEIR IDENTITY IN HYBRIDS. GENES ARE NEVER BLENDED TOGETHER.



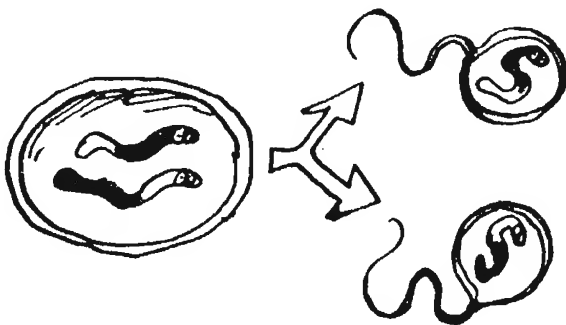
NO COMPROMISE WITH RECESSIVES!

2 ONE FORM ("ALLELE") OF A GENE MAY BE DOMINANT OVER ANOTHER. BUT RECESSIVE GENES WILL POP UP LATER!!



THE SECRET OF MY SPECKLED GOATS!

3 EACH ADULT ORGANISM HAS TWO COPIES OF EACH GENE — ONE FROM EACH PARENT. WHEN POLLEN OR SPERM AND EGGS ARE PRODUCED, THEY EACH GET ONE COPY.



4 DIFFERENT ALLELES ARE SORTED OUT TO SPERM AND EGG RANDOMLY AND INDEPENDENTLY. ALL COMBINATIONS OF ALLELES ARE EQUALLY LIKELY:

AABBCCDDEEFFGGHH
AaBBCCDDEEFFGGHH
aaBBCCDDEEFFGGHH
AA BBCCDDEEFFGGHH
AA BbCCDDEEFFGGHH
Aa BbCCDDEEFFGGHH
aa BbCCDDEEFFGGHH
ETC!

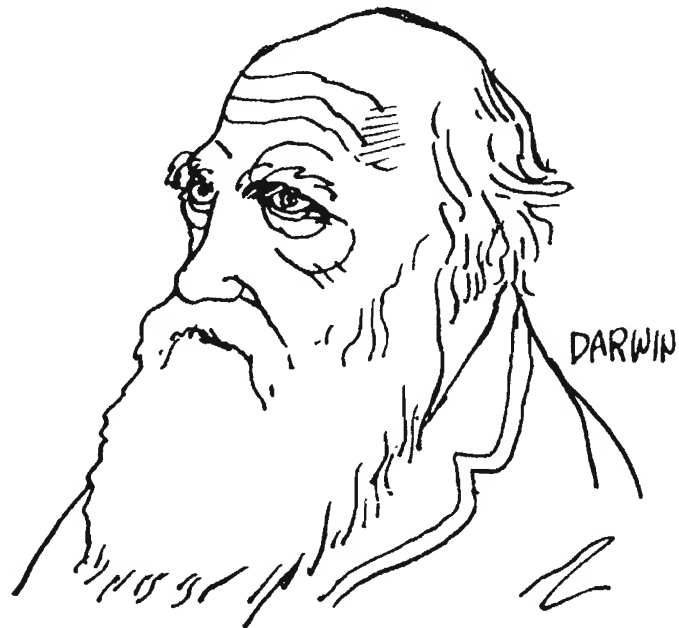


WE'LL SEE SHORTLY THAT NOT ALL THESE POINTS ARE EXACTLY CORRECT... DOMINANCE IS SOMETIMES ONLY PARTIAL... THERE ARE ORGANISMS WITH ONLY A SINGLE SET OF GENES... AND SOME WITH FOUR SETS... AND DEVIATIONS FROM INDEPENDENT ASSORTMENT TURN OUT TO BE VERY IMPORTANT...

MENDEL PRESENTED HIS THEORY IN 1865 TO THE BRÜNN NATURAL SCIENCE SOCIETY... IT PUT THEM TO SLEEP.



UNFORTUNATELY, NOBODY CARED ABOUT THE PROBLEM ANY MORE... IT HAD GONE OUT OF FASHION... AND, BESIDES, SINCE 1859, BIOLOGISTS HAD BEEN DISTRACTED BY THE NEW THEORY OF EVOLUTION, AND COULDN'T BE BOTHERED WITH MENDEL'S EQUATIONS.



BY THE TIME MENDEL DIED, THE SCIENTIFIC COMMUNITY HAD TOTALLY FORGOTTEN HIS WORK. "MY TIME WILL COME," HE SAID, NOT LONG BEFORE HIS DEATH IN 1884...

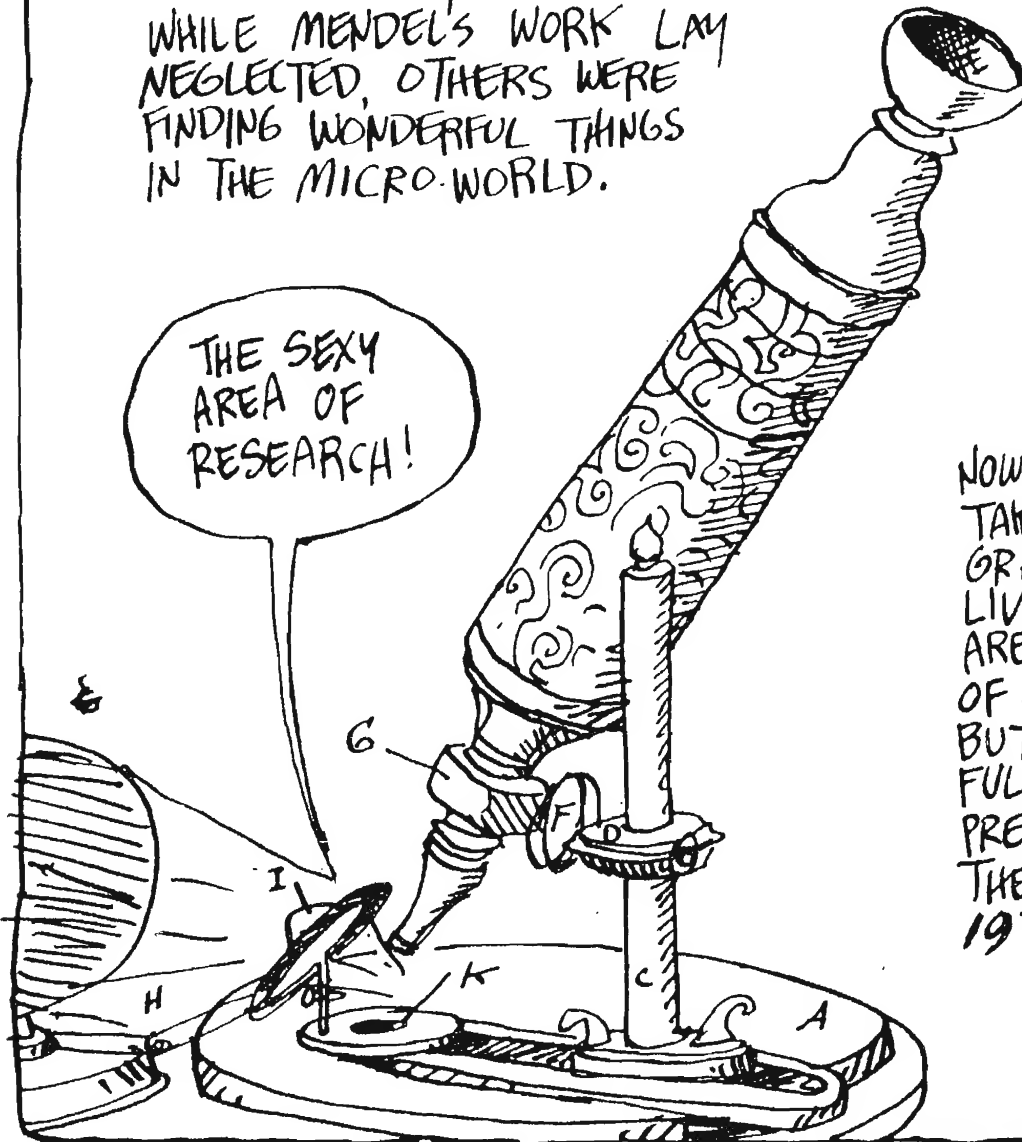


NOW YOU SEE THEM...

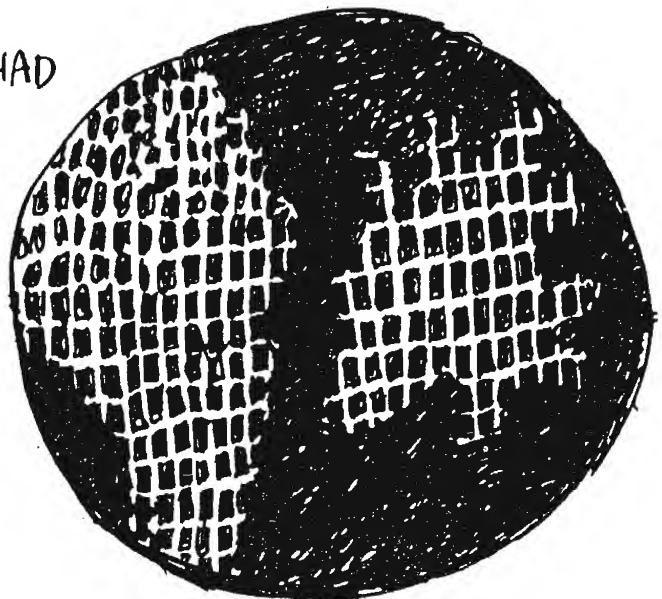
WHILE MENDEL'S WORK LAY
NEGLECTED, OTHERS WERE
FINDING WONDERFUL THINGS
IN THE MICRO-WORLD.

THE SEXY
AREA OF
RESEARCH!

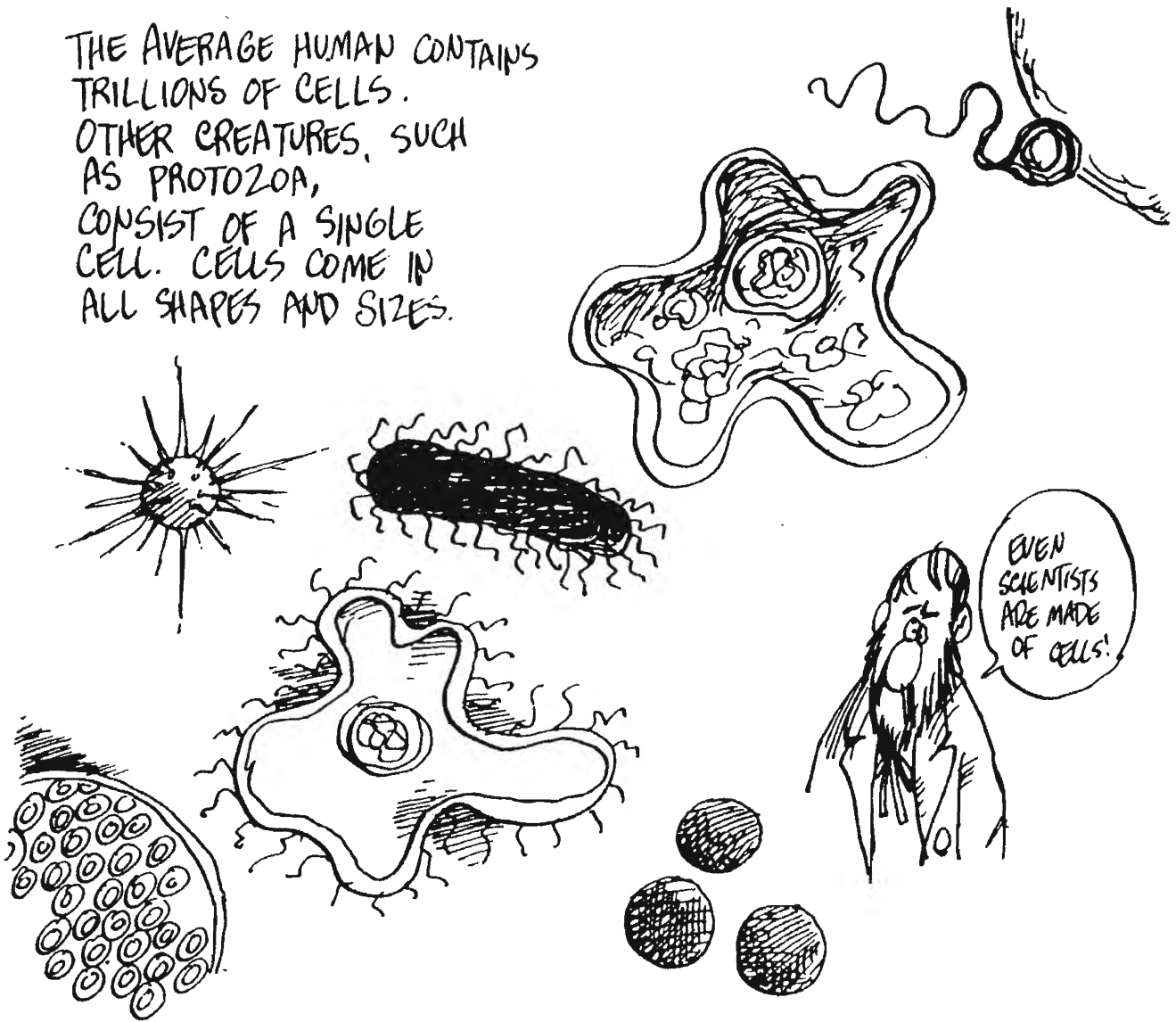
NOWADAYS, WE
TAKE IT FOR
GRANTED THAT ALL
LIVING THINGS
ARE MADE UP
OF **CELLS** —
BUT THIS WASN'T
FULLY AP-
PRECIATED UNTIL
THE LATE
19TH CENTURY.



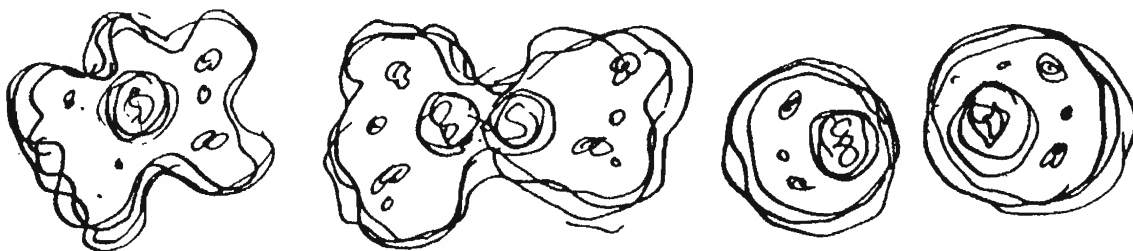
AS FAR BACK AS THE 1600'S,
ROBERT HOOKE (1635-1703) HAD
NOTICED THE CELLULAR
STRUCTURE OF CORK.
BUT IT WASN'T UNTIL THE
1800'S THAT SCIENTISTS,
ARMED WITH BETTER
MICROSCOPES, REALIZED
THAT ALL OF US ARE
DIVIDED INTO LITTLE
COMPARTMENTS.



THE AVERAGE HUMAN CONTAINS TRILLIONS OF CELLS. OTHER CREATURES, SUCH AS PROTOZOA, CONSIST OF A SINGLE CELL. CELLS COME IN ALL SHAPES AND SIZES.



MOREOVER, SCIENTISTS SAW THAT ALL CELLS COME FROM THE **DIVISION** OF A PRE-EXISTING CELL. BEFORE DIVISION, EVERYTHING IN THE CELL IS DOUBLED.

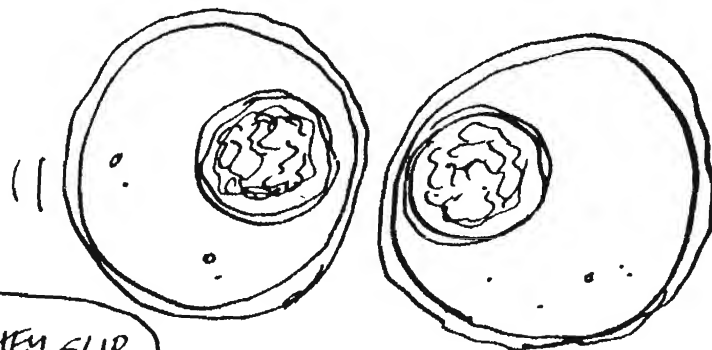
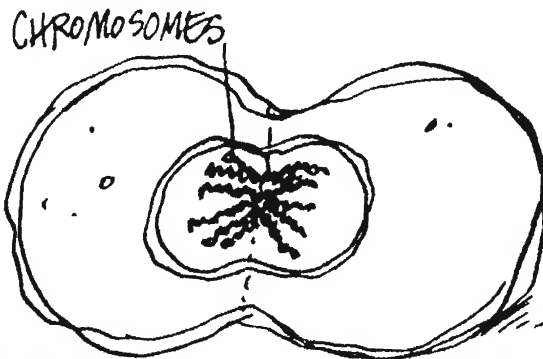
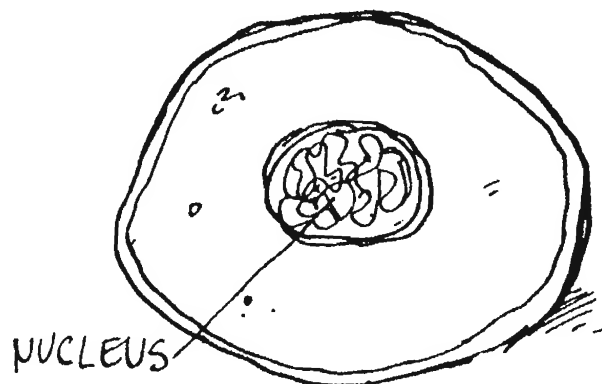


AS MICROSCOPES IMPROVED, THE CELL'S INTERNAL STRUCTURE EMERGED...

FIRST OF ALL, THERE WAS THE **NUCLEUS** — AND WITHIN THE NUCLEUS WAS SOMETHING WEIRD...

JUST BEFORE CELL DIVISION, SOME SHORT, STRINGY OBJECTS SUDDENLY APPEARED, DOUBLED, AND THEN VANISHED!

THESE WERE DUBBED "**CHROMOSOMES**" AND WERE THE CAUSE OF MUCH DEBATE !!



CHROMOSOMES ARE LIKE CAMPAIGN PROMISES — THEY MATERIALIZE FROM THE AIR AND THEN DISAPPEAR...

THEY SLIP IN AND OUT THE BACK DOOR — LIKE A MILKMAN!

ONLY ONE WAY TO FIND OUT...

CONSULT AN EXPERT!

AN EXPERT IN CELLS?

NO... AN EXPERT IN DISAPPEARANCES!

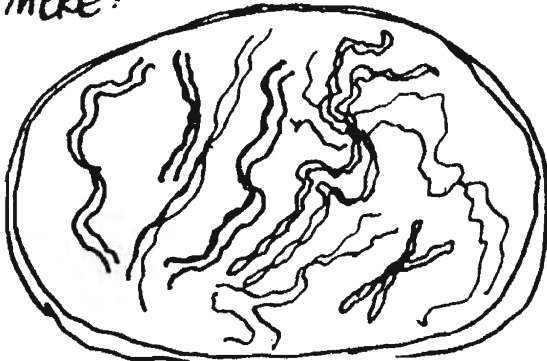
ONLY ONE POSSIBILITY, GENTS!

THEY WERE THERE ALL ALONG!

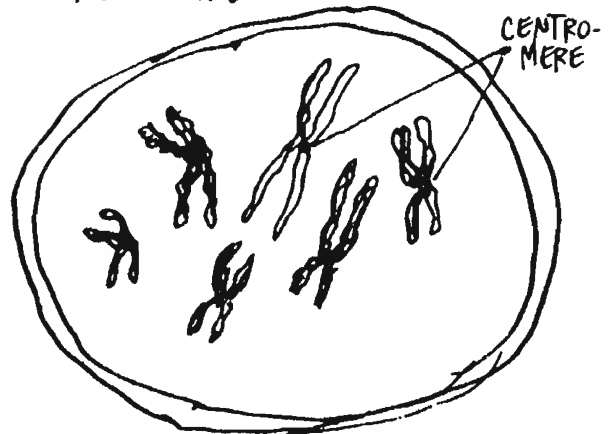
IT WAS FINALLY AGREED — CHROMOSOMES DON'T REALLY DE-MATERIALIZE OR DISSOLVE... THEY'RE JUST TOO **SKINNY** MOST OF THE TIME TO BE VISIBLE WITH A CONVENTIONAL MICROSCOPE. DURING CELL DIVISION, HOWEVER, THEY **COIL UP**, BECOMING THICK ENOUGH TO SEE.

CAREFUL STUDY REVEALED WHAT HAPPENS TO CHROMOSOMES DURING CELL DIVISION.

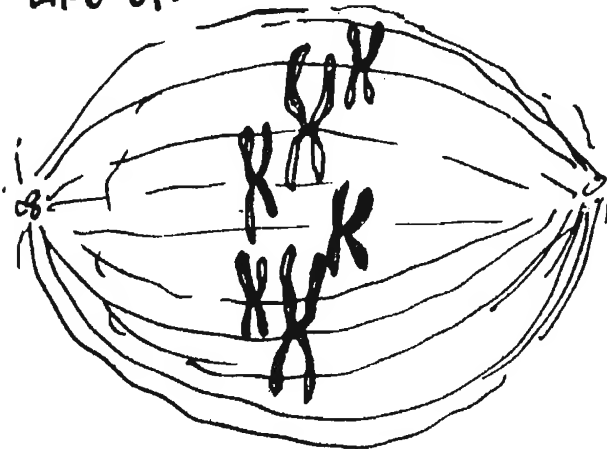
FIRST—WHILE STILL INVISIBLE—THE CHROMOSOMES DUPLICATE THEMSELVES, REMAINING ATTACHED AT A SPOT CALLED THE CENTROMERE:



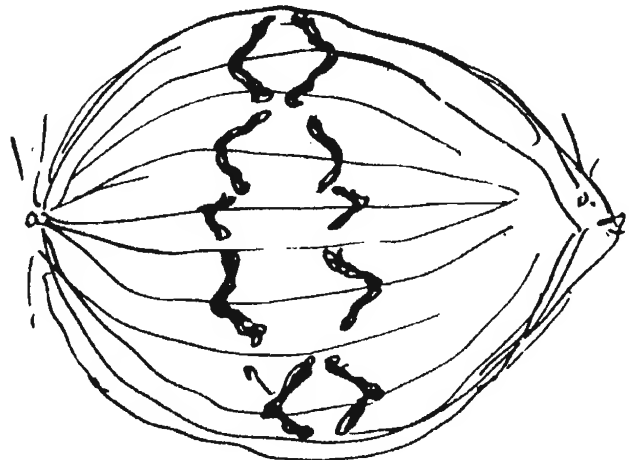
NEXT THEY THICKEN AND SHORTEN, BECOMING VISIBLE UNDER THE MICROSCOPE.



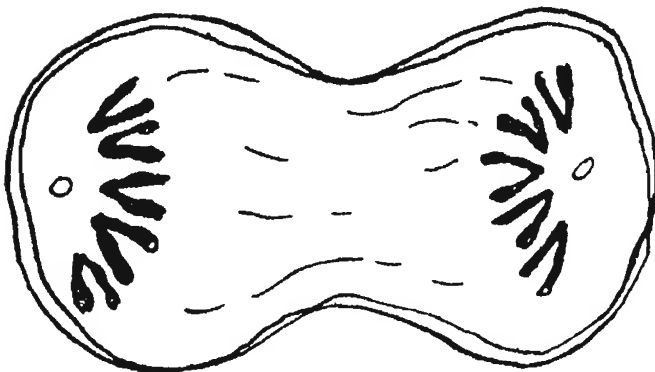
THE MEMBRANE AROUND THE NUCLEUS DISSOLVES, AND A FIBROUS SPINDLE FORMS, ON WHICH THE CHROMOSOMES LINE UP.



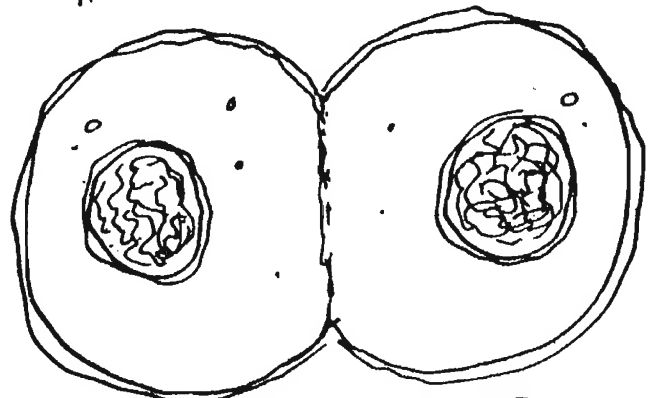
THE CENTROMERES DIVIDE AS THE SPINDLE FIBERS TUG THE CHROMOSOME PAIRS APART.



THE CHROMOSOMES ARRIVE AT THE OPPOSITE POLES, AND THE SPINDLE DISPERSES.

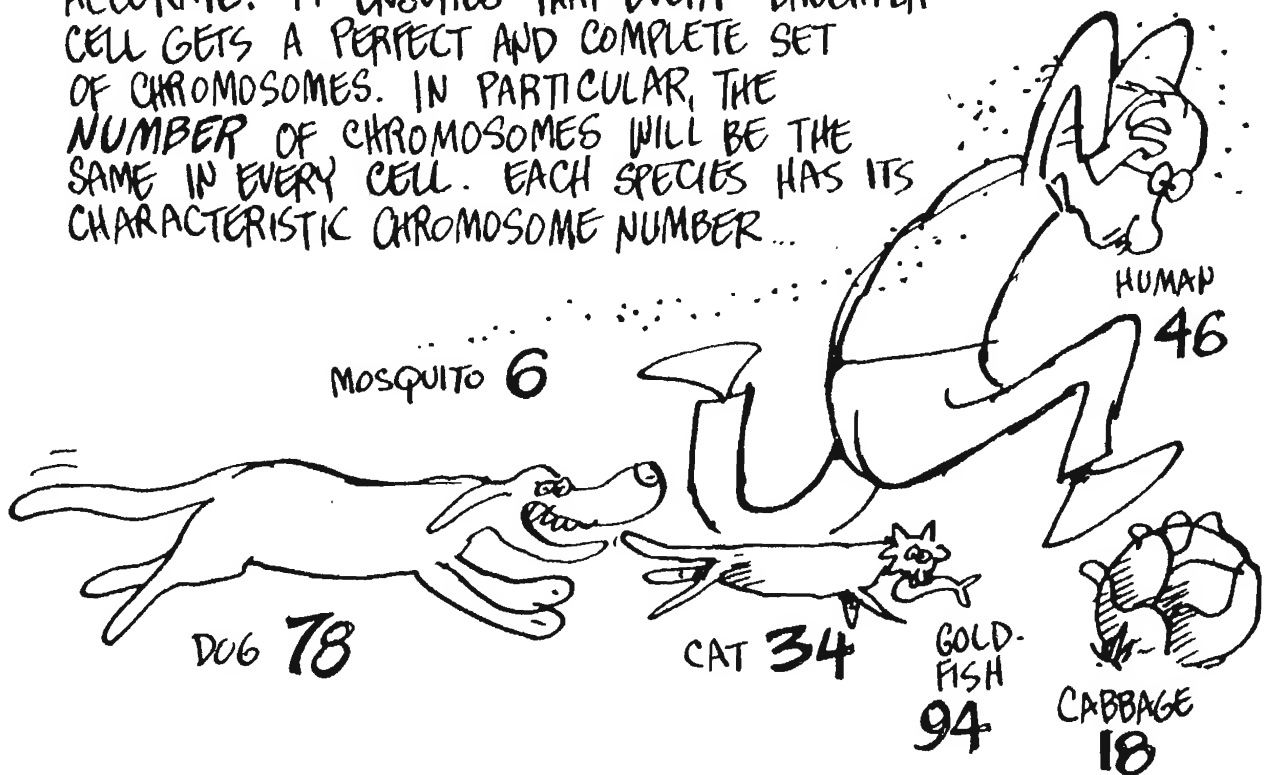


THE NUCLEAR MEMBRANE RE-FORMS; THE CHROMOSOMES UNWIND INTO INVISIBILITY; AND THE CELL DIVIDES.

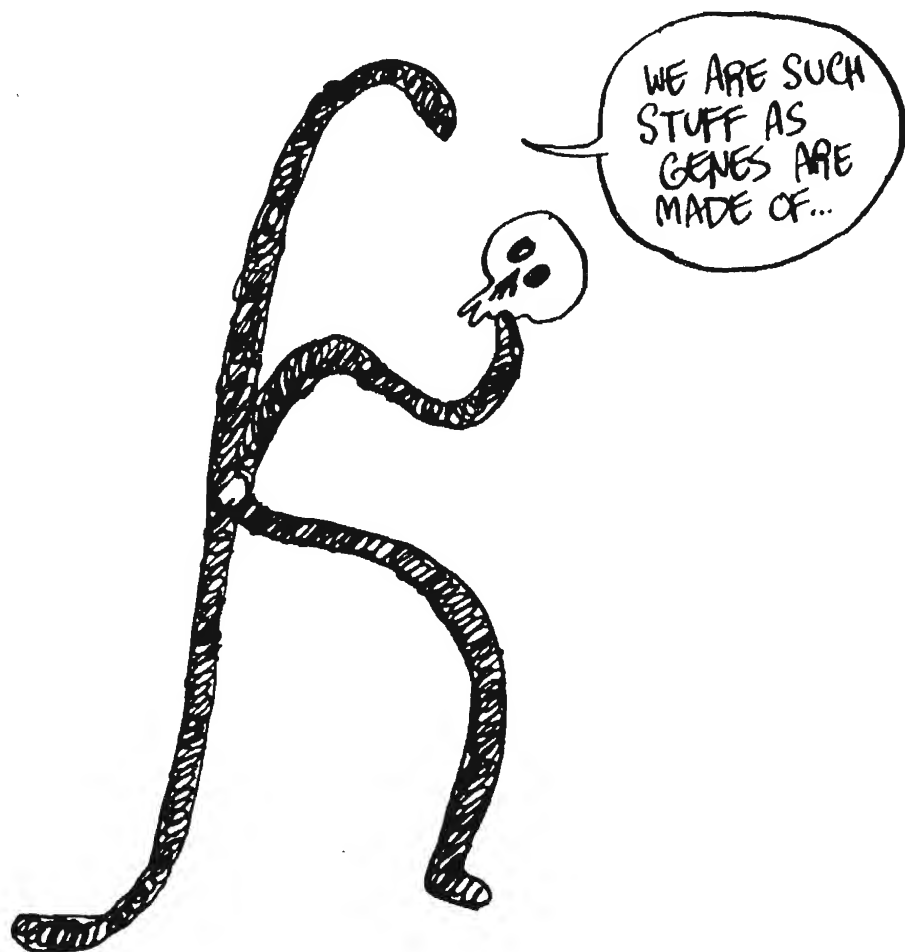


THIS PROCESS IS CALLED **MITOSIS**.

THE PROCESS OF MITOSIS IS EXTREMELY ACCURATE. IT ENSURES THAT EVERY "DAUGHTER" CELL GETS A PERFECT AND COMPLETE SET OF CHROMOSOMES. IN PARTICULAR, THE **NUMBER** OF CHROMOSOMES WILL BE THE SAME IN EVERY CELL. EACH SPECIES HAS ITS CHARACTERISTIC CHROMOSOME NUMBER...



YOU MAY HAVE NOTICED THAT ALL THESE NUMBERS ARE EVEN. THERE IS A GOOD REASON FOR THIS — A REASON THAT POINTS TO THE CHROMOSOMES AS THE VERY MATERIAL OF HEREDITY ITSELF!



IT WAS THIS

FACT!

SPERM AND EGG ARE
SINGLE CELLS WITH
ONLY HALF THE NORMAL
NUMBER OF CHROMOSOMES.

DAZZLING!

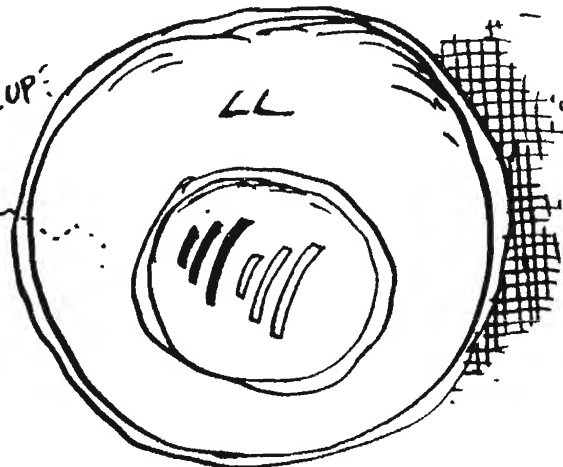


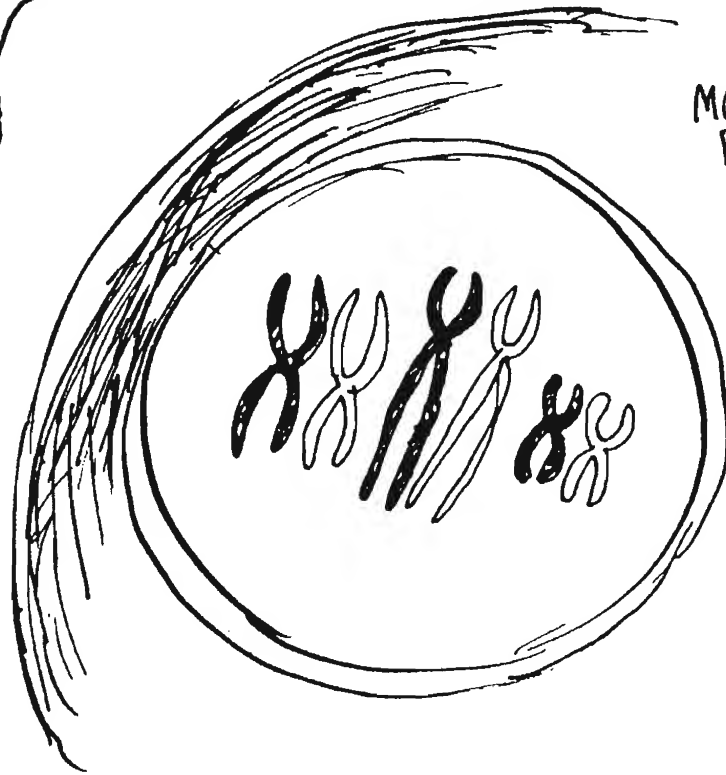
PUSHY!

IT WORKS LIKE THIS:
THE SPERM AND EGG—
THE GERM CELLS, OR
GAMETES, AS THEY
ARE KNOWN—EACH
CARRIES A HALF SET
OF CHROMOSOMES.

AT FERTILIZATION, THEIR
NUCLEI UNITE, GIVING
THE FERTILIZED EGG,
OR **ZYGOTE**, A FULL
COMPLEMENT OF CHROMOSOMES.
FROM THIS CELL ARISE
ALL OTHERS BY MITOSIS.

GLUP!

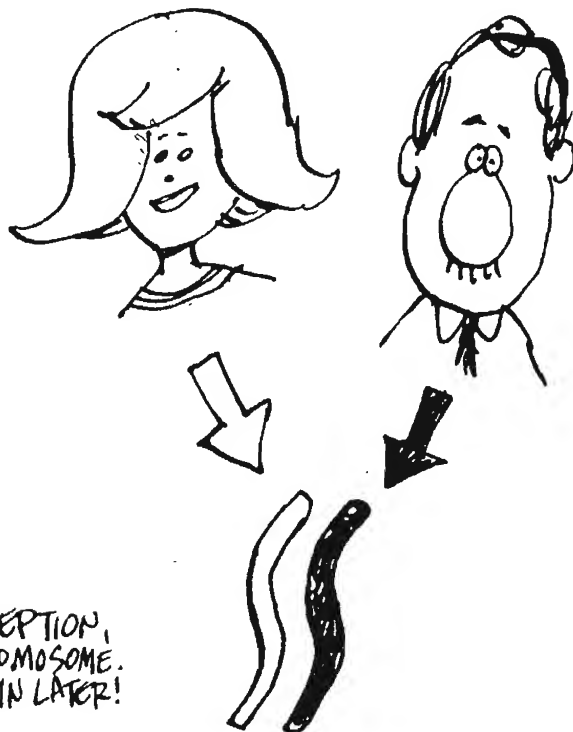




MOREOVER, IT WAS DISCOVERED (BY THE AMERICAN WILLIAM SUTTON IN 1902) THAT EACH CHROMOSOME FROM THE SPERM CAN BE MATCHED WITH A VIRTUALLY IDENTICAL ONE FROM THE EGG. (IT'S EASIER TO SEE WHEN THEY'RE DOUBLED AND CONTRACTED.)

THUS, THERE ARE REALLY ALREADY TWO COPIES OF EVERY CHROMOSOME IN THE CELL. THESE ARE CALLED "**HOMOLOGOUS PAIRS**"—"HOMOLOGOUS" MEANING "SAME SHAPE."

HUMANS, FOR EXAMPLE, WITH 46 CHROMOSOMES, REALLY HAVE 23* HOMOLOGOUS PAIRS: ONE FROM EACH PAIR COMES FROM MOM AND ONE FROM DAD.

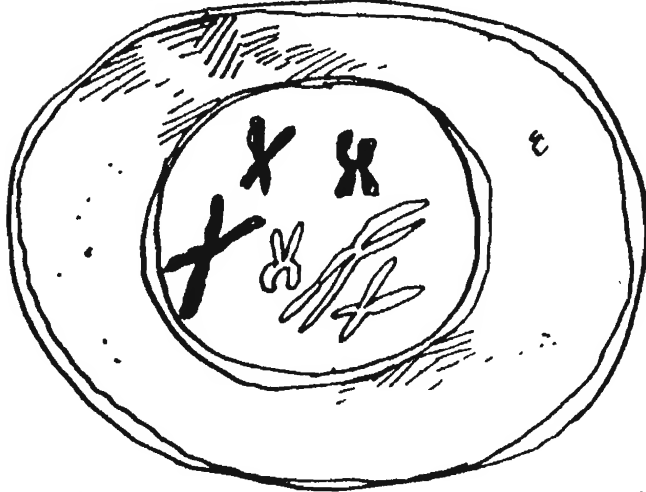


*WITH ONE EXCEPTION, THE SEX CHROMOSOME. WE'LL EXPLAIN LATER!

THIS SUGGESTS THAT THERE MUST BE A SPECIAL KIND OF CELL DIVISION JUST FOR MAKING GAMETES...

THIS PROCESS, CALLED **MEIOSIS**, IS ACTUALLY A **DOUBLE** DIVISION:

AS IN MITOSIS, THE CHROMOSOMES DOUBLE AND THICKEN:



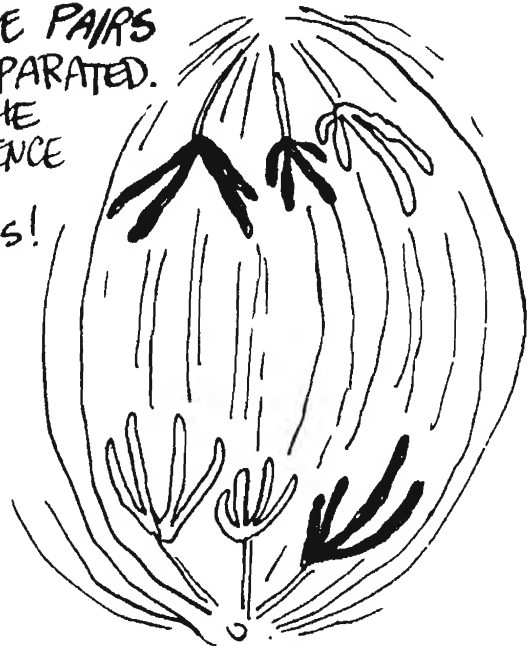
BUT THEN THE **HOMOLOGOUS** CHROMOSOMES PAIR OFF -- SOMEHOW!



AGAIN THE SPINDLE FIBERS FORM AND THE CHROMOSOME QUARTETS ("TETRADS") LINE UP...



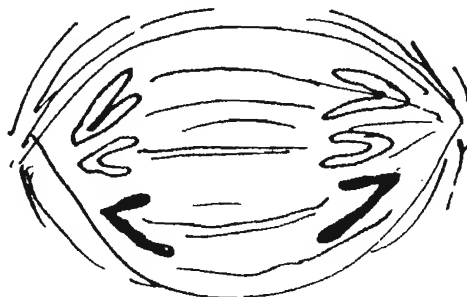
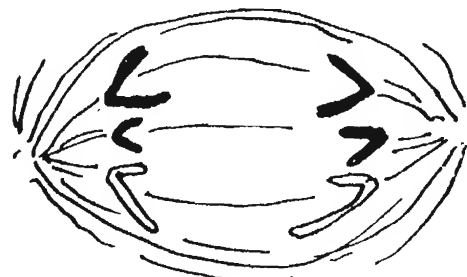
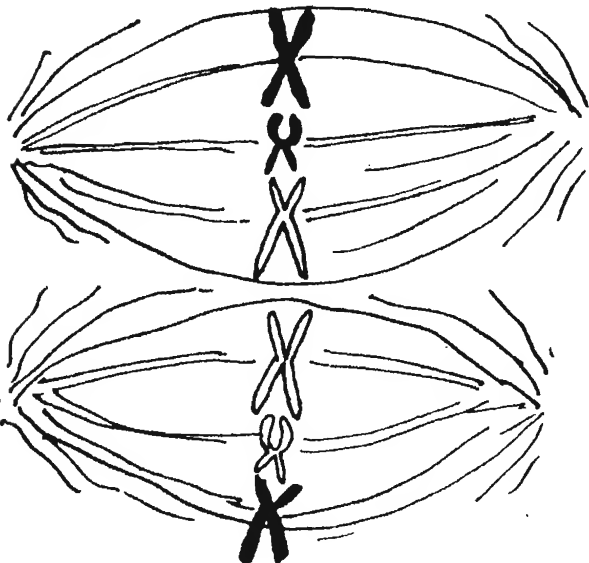
AND THE PAIRS ARE SEPARATED. NOTE THE DIFFERENCE FROM MITOSIS!



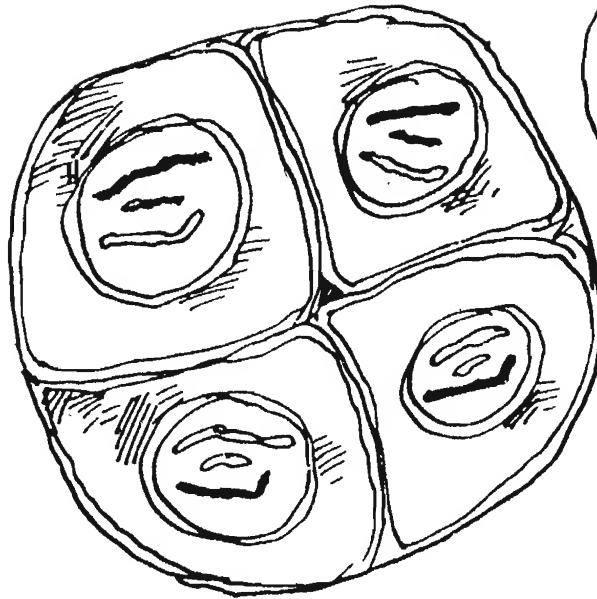
(MORE ON THIS LATER!)

WHEN THEY REACH THE POLES, THE SPINDLE VANISHES AND **NEW** SPINDLES FORM "THE OTHER WAY."

THE CHROMOSOMES THEN SEPARATE, AS IN MITOSIS.



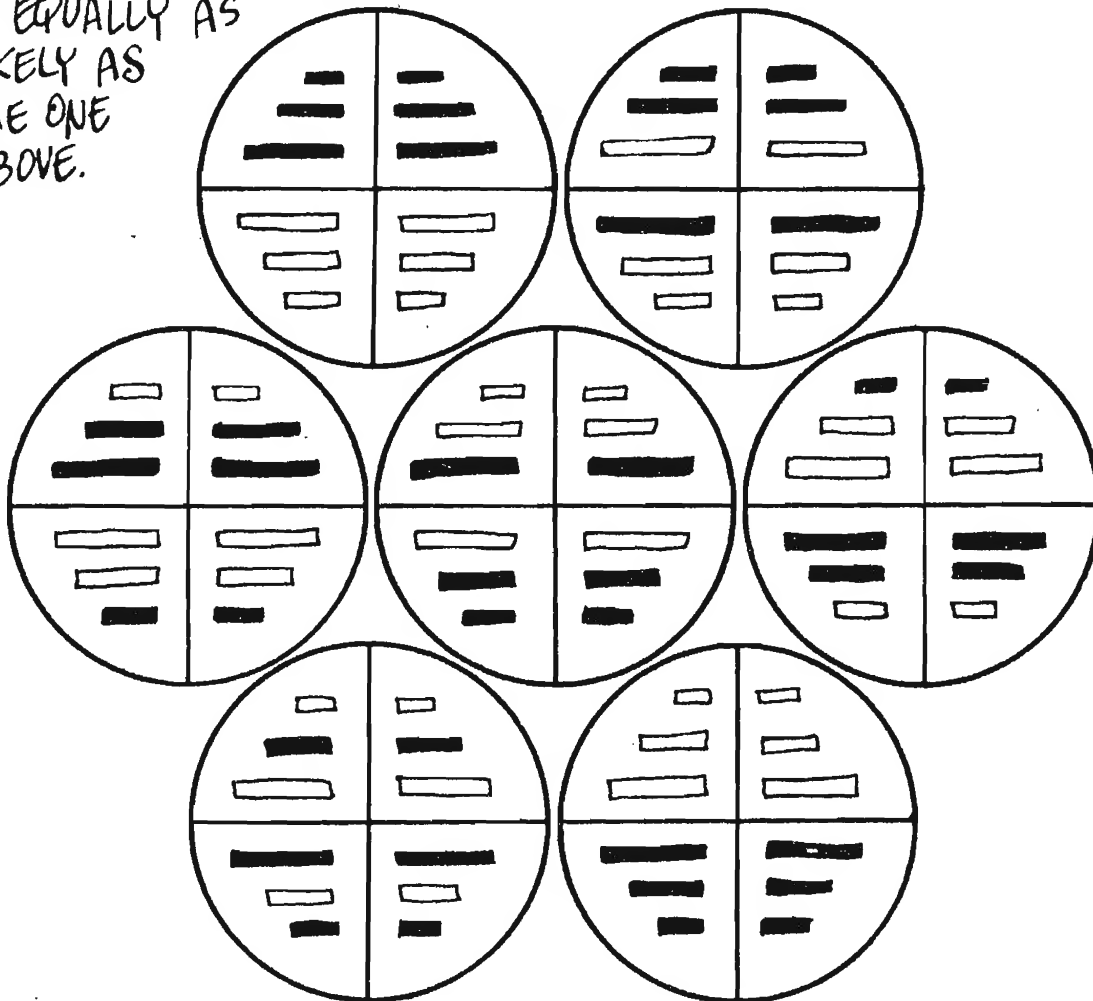
MEIOSIS RESULTS
IN **FOUR** CELLS,
EACH WITH **HALF**
THE CHROMOSOMES
OF THE ORIGINAL.
COUNT 'EM —
3 VS. 6 IN THIS
CASE.



BUT ALWAYS
ONE FROM EACH
HOMOLOGOUS
PAIR!



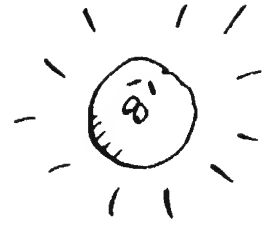
NOTE THAT WHICH COPY ("HOMOLOG") OF EACH CHROMOSOME GOES
TO WHICH CELL IS COMPLETELY RANDOM.
EACH OF THESE COMBINATIONS
IS EQUALLY AS
LIKELY AS
THE ONE
ABOVE.



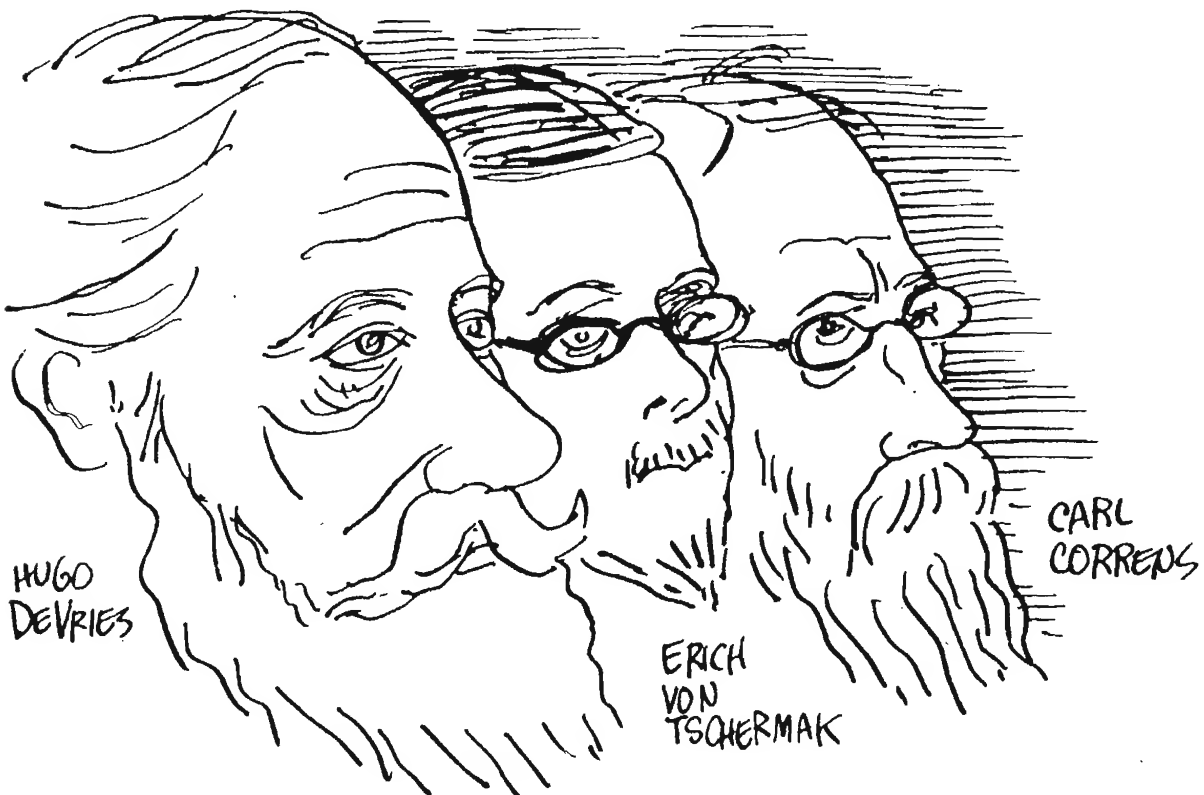
THAT IS, THE CHROMOSOMES OBEY THE LAW OF
INDEPENDENT ASSORTMENT.



ONCE MEIOSIS AND MITOSIS WERE UNDERSTOOD, BIOLOGISTS BEGAN TO SUSPECT THAT CHROMOSOMES MIGHT GOVERN HEREDITY... THEY LOOKED AGAIN AT PATTERNS OF INHERITANCE... AND SCIENCE AGAIN MARCHED — BACKWARD, TO THE LAWS OF MENDEL!!



TOWARD THE END OF THE 19TH CENTURY, THREE SCIENTISTS, WORKING INDEPENDENTLY, MORE OR LESS DUPLICATED THE AUSTRIAN MONK'S EXPERIMENTS AND RESULTS. THEY WERE:



IN THE YEAR 1900, ALL THREE SEARCHED THE SCIENTIFIC LIBRARIES FOR PRECURSORS OF THEIR OWN WORK, AND ALL FOUND GREGOR MENDEL!



AFTER THEY HAD FINISHED KICKING THEMSELVES, DEVRIES, CORRENS, AND TSCHERMAK ANNOUNCED MENDEL'S DISCOVERY TO THE WORLD. WITHIN TWO YEARS, WILLIAM SUTTON HAD SEEN HOMOLOGOUS PAIRS OF CHROMOSOMES IN GRASSHOPPER CELLS, AND SCIENCE HAD SEEN THE LIGHT!!



TO SUMMARIZE:

WHAT **EXACTLY** DID THEY **REALIZE**?

ANSWER:



CHROMOSOMES BEHAVE LIKE GENES. THEY RETAIN THEIR IDENTITY IN HYBRIDS, AND THEY SEGREGATE INDEPENDENTLY WHEN GERM CELLS ARE MADE. THEREFORE, IT'S LOGICAL TO ASSUME THAT GENES LIE ON CHROMOSOMES. (THERE MUST BE MANY GENES ON EACH ONE, BECAUSE THERE MUST BE FAR MORE GENES THAN THE FEW DOZEN CHROMOSOMES TYPICAL OF MOST SPECIES.)

A B c d E f ETC!

THE DISCOVERY OF HOMOLOGOUS PAIRS REALLY CINCHED THE CONNECTION TO MENDEL'S FINDINGS. REMEMBER, EACH CELL HAS A PAIR OF ALLELES FOR EACH GENE. NOW IT WAS REALIZED THAT:



**THE TWO COPIES OF
A GIVEN GENE LIE AT
THE SAME POINT ON
HOMOLOGOUS CHROMOSOMES.**

I.E., IF
ONE GENE
FOR HEIGHT
LIES
HERE →



THEN
THE OTHER
COPY MUST
BE
HERE ←

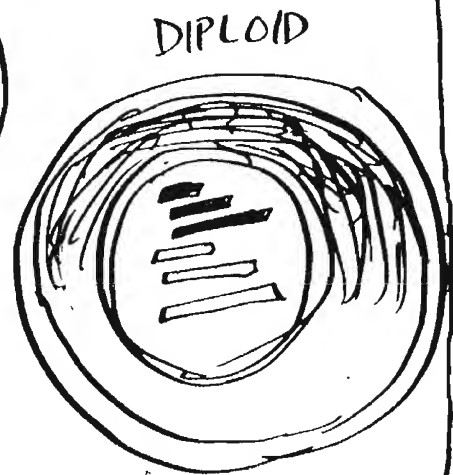
ALL THIS TURNS OUT TO BE TRUE... BUT ONCE PEOPLE LOOKED MORE DEEPLY INTO THE MATTER, THEY DISCOVERED A FEW THINGS MENDEL HADN'T REALIZED...

FOR ONE THING, NOT ALL ORGANISMS HAVE A DOUBLE SET OF CHROMOSOMES. MANY LOWER SPECIES, LIKE SOME FUNGI, HAVE JUST A SINGLE SET.

LOWER
THAN
WHOM?



A CELL WITH A SINGLE SET OF CHROMOSOMES IS CALLED **HAPLOID**; ONE WITH TWO SETS IS CALLED **DIPLOID**. OUR BODY CELLS ARE DIPLOID, WHILE OUR GERM (SEX) CELLS ARE HAPLOID.



DIPLOID ORGANISMS INCLUDE ALL THE FAMILIAR MAMMALS AND BIRDS AND MANY PLANTS. HAPLOIDS INCLUDE MALE HONEY BEES, MANY FUNGI, AND ASEXUAL ONE-CELLED CREATURES.

BESIDES ALL THESE, THERE ARE ALSO **POLYPLOID** ORGANISMS, WITH MULTIPLE SETS OF CHROMOSOMES. A SURPRISING NUMBER OF EVERYDAY PLANTS ARE POLYPLOID. (NOT PEAS, THOUGH!!)

LIKE THE
POTATO!



THE OTHER MAIN PROBLEM WITH MENDEL'S THEORY WAS THE PRINCIPLE OF INDEPENDENT ASSORTMENT. A PRECISE MEASURE OF HOW WRONG IT WAS LED TO THE ABILITY TO MAP OUT EXACTLY WHERE ON THE CHROMOSOME EACH OF ITS GENES MIGHT LIE... READ ON...



MAPMAKING

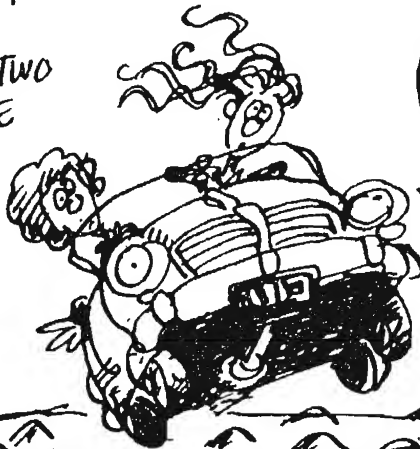
TO MENDEL—AND HIS
HEIRS—GENES WERE
JUST ABSTRACTIONS,
LETTERS YOU COULD JUGGLE
TO EXPLAIN AND PREDICT
HOW HEREDITARY QUALITIES
WOULD BE PASSED
ALONG TO FUTURE
GENERATIONS.

NOW IT APPEARED THAT
GENES WERE ACTUAL,
PHYSICAL OBJECTS. THEY
LAY IN SOME ORDER ALONG
THE CHROMOSOMES OF
EVERY CELL, AND THE TWO
ALLELES OF EACH GENE
WERE ON THE TWO
CHROMOSOMES OF A
HOMOLOGOUS PAIR.

THEY'RE LIKE
GHOSTS—
INFLUENTIAL
BUT
INSUBSTANTIAL!



THEY'RE
AS REAL AS
BUMPS IN
THE ROAD!



99

ONE MIGHT WONDER
IF IT'S POSSIBLE TO
MAKE A **GENE MAP**
SHOWING JUST WHERE
ON EACH CHROMO-
SOME ALL THESE
HEREDITARY UNITS
MIGHT LIE!!



THE ANSWER TO THIS DEPENDS ON A SEEMING **PARADOX**, FOR IN ONE RESPECT MENDEL'S FINDINGS CONFLICTED WITH THE OBSERVED BEHAVIOR OF CHROMOSOMES...



NAMELY —
THE PRINCIPLE OF
INDEPENDENT
ASSORTMENT!

OBSERVE: THE NUMBER OF GENES MUST BE TREMENDOUS TO GOVERN A COMPLEX ORGANISM, BUT THE NUMBER OF CHROMOSOMES IN A CELL IS FAIRLY SMALL. A PEA PLANT HAS JUST **7 PAIRS** OF CHROMOSOMES, A HUMAN **23**.

CONCLUSION:
MANY GENES
ON EACH
CHROMOSOME!



THE PROBLEM: IF TWO GENES LIE ON THE SAME CHROMOSOME, **HOW CAN THEY BE INDEPENDENT??** AFTER ALL, CHROMOSOMES DON'T BREAK APART, DO THEY? SHOULDN'T DIFFERENT GENES SOMETIMES BE **LINKED??**

PHYSICALLY
LINKED — BY THE
CHROMOSOME!



SO — DO GENES
ASSORT INDEPEN-
DENTLY OR NOT?

WELL, IT TURNED OUT
TO BE SORT OF HALF-AND-HALF...



THERE IS LINKAGE BETWEEN CERTAIN
GENES....

BUT



CHROMOSOMES ALSO ENGAGE IN A
GOOD DEAL OF **GENE SWAPPING**,
OR (AS IT'S CALLED) **CROSSING OVER**.

TO ILLUSTRATE, LET'S LOOK
AT THE EXAMPLE OF THE
ORDINARY, GARDEN-VARIETY
TOMATO.



WITH MUTANT
MAYONNAISE?

...AND TRY NOT TO EAT
THE EXAMPLE UNTIL
AFTER CLASS...

TOMATOES HAVE A SKIN-TEXTURE GENE WITH A RECESSIVE ALLELE, p , WHICH CAUSES HAIRY FRUIT. (OF COURSE, YOU DON'T OFTEN SEE THESE IN THE MARKET!)



LIKEWISE, THE HEIGHT GENE HAS A RECESSIVE ALLELE, d , CAUSING DWARF PLANTS.



TO TEST THE PRINCIPLE OF INDEPENDENT ASSORTMENT, WE CAN CROSS A DOUBLE RECESSIVE, $ppdd$, WITH A HETEROZYGOTE, pp^+dd^+ .

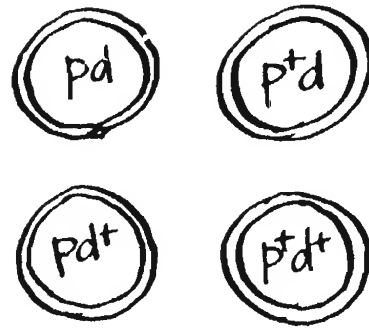
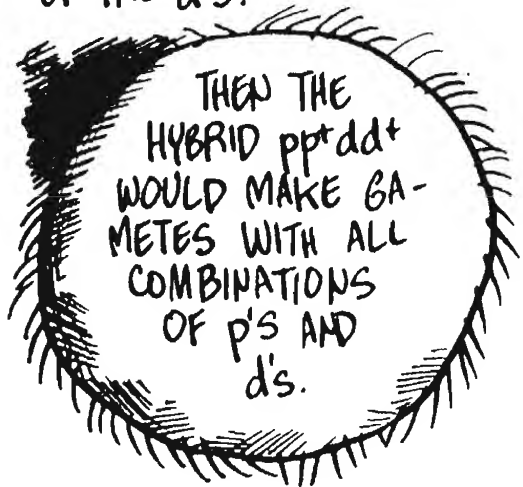


HAIRY, DWARF
 $ppdd$

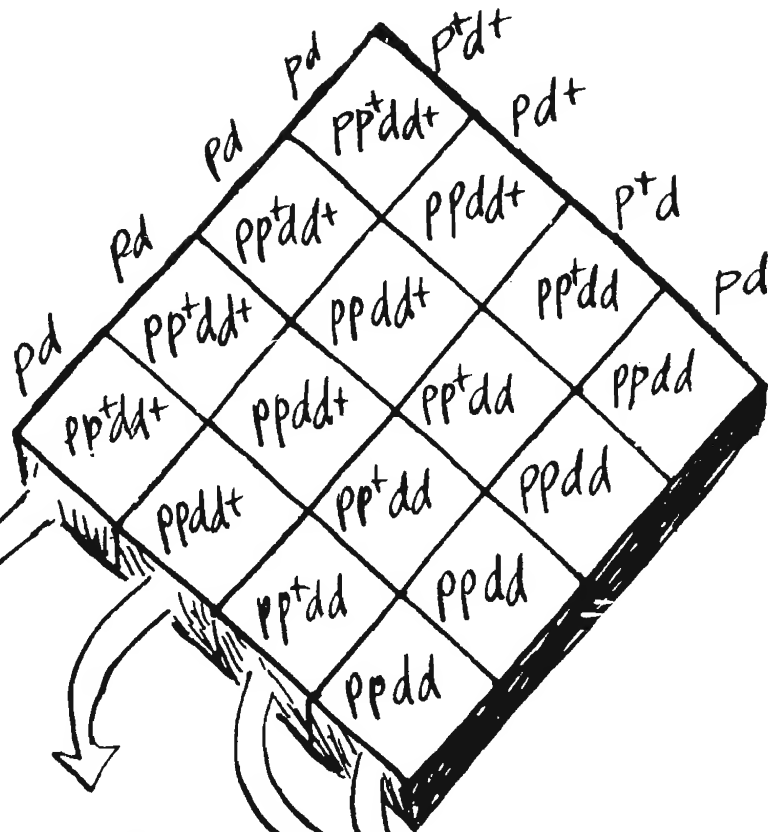


SMOOTH, TALL
 pp^+dd^+

SUPPOSE MENDEL WAS RIGHT, AND THE p's WERE INDEPENDENT OF THE d's.



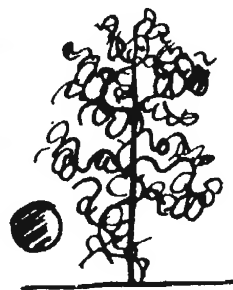
CROSSING WITH THE DOUBLE RECESSIVE ppdd GIVES THIS:



$\frac{1}{4}$ SMOOTH, TALL



$\frac{1}{4}$ HAIRY, TALL

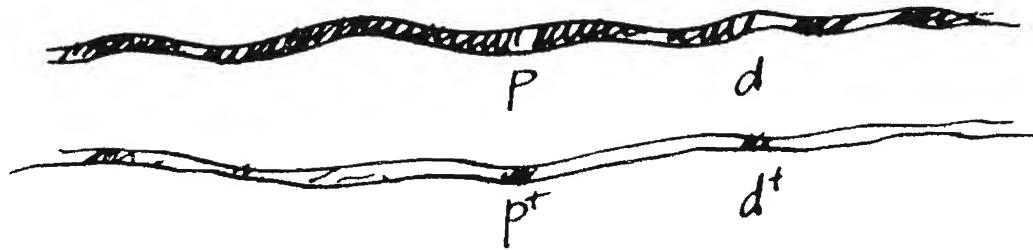


$\frac{1}{4}$ SMOOTH, DWARF

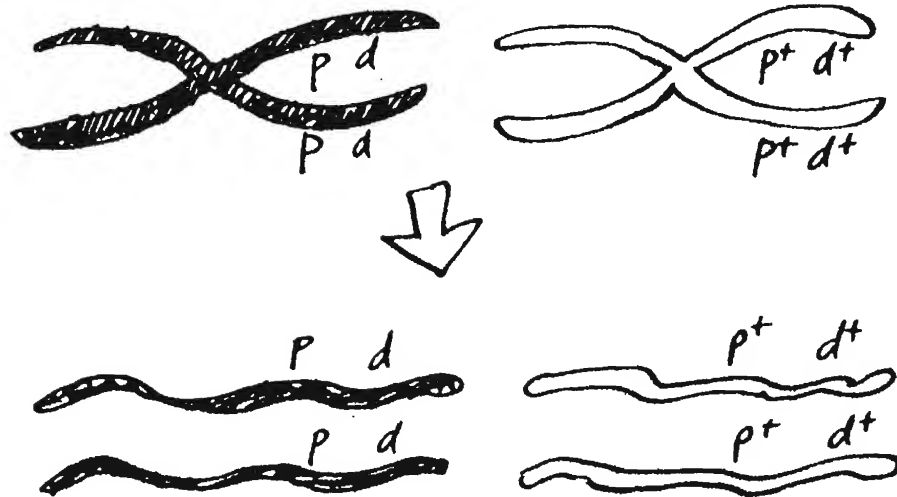


$\frac{1}{4}$ HAIRY, DWARF

NOW SUPPOSE p AND d LIE ON THE SAME CHROMOSOME:
 THEN THE HYBRID pp^+dd^+ HAS ITS ALLELES ON A
 HOMOLOGOUS PAIR:



DURING
 MEIOSIS,
 THEY
 ARE
 SORTED
 OUT
 LIKE
 THIS:



IN THIS CASE, ONLY TWO TYPES OF GAMETES CAN BE MADE:
 pd AND p^+d^+ , RATHER THAN THE FOUR PREDICTED BY MENDEL.

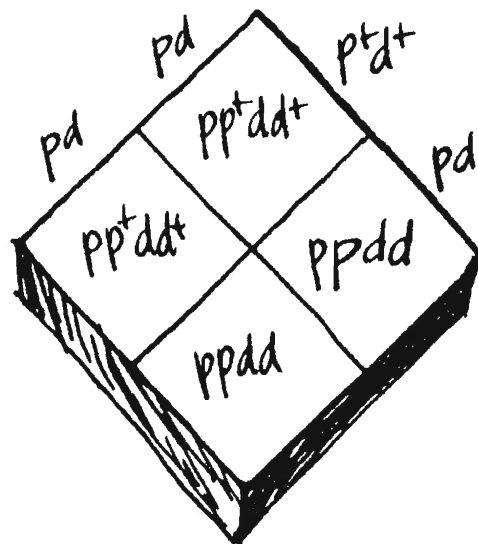
CROSSING WITH THE DOUBLE
 RECESSIVE $ppdd$, WE GET



$\frac{1}{2}$ SMOOTH, TALL
 pp^+dd^+



$\frac{1}{2}$ HAIRY, DWARF
 $ppdd$



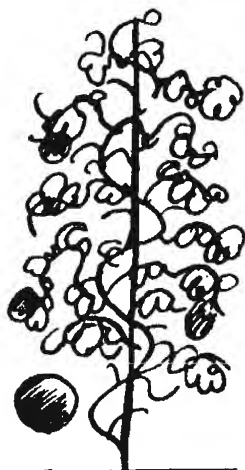


AND OF COURSE,
WHO'S ON THE
SIDE OF THE
ANGELS?

WHEN THE CROSS IS
ACTUALLY MADE,
WHAT DOES ONE
ACTUALLY GET: A 50:50
SPLIT OR AN EQUAL
4-WAY SPLIT?

IT SEEMS THAT **NEITHER**
PREDICTION IS CORRECT.
ALL FOUR TYPES DO
APPEAR, BUT IN THESE
PROPORTIONS:

SORRY, GREG!



SMOOTH, TALL
 pp^+dd^+
48%



HAIRY, TALL
 $ppdd^+$
2%



SMOOTH, DWARF
 pp^+dd
2%



HAIRY, DWARF
 $pp\ dd$
48%

IT'S O.K.,
I CAN TAKE THE
DISAPPOINTMENT...

AFTER ALL,
I AM DEAD -

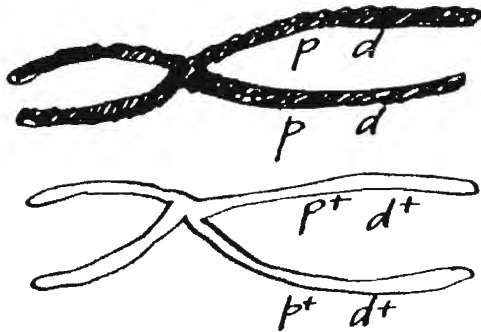
SORRY!



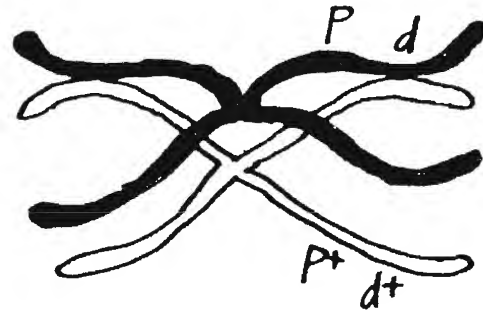
IT'S CERTAINLY
CLOSER TO THE
PREDICTION BASED ON
LINKAGE THAN TO
MENDEL'S. BUT IF
P. AND d ARE
LINKED, THEN
WHERE DID THOSE
2% COMBINATIONS
COME FROM??

NOT TO PROLONG THE MYSTERY — THE GENES p AND d ARE ON THE SAME CHROMOSOME, BUT CHROMOSOMES CAN EXCHANGE GENES. IT'S CALLED CROSSING OVER:

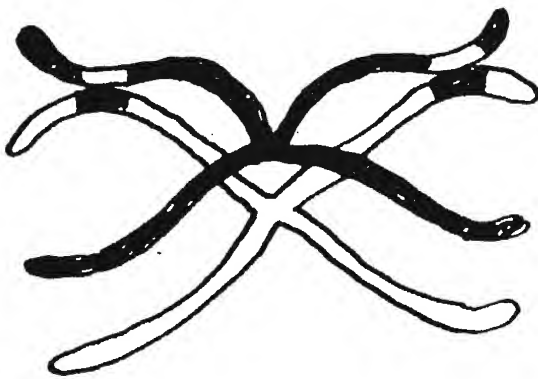
DURING MEIOSIS, HOMOLOGUES LINE UP WITH CORRESPONDING ALLELES OPPOSITE ONE ANOTHER.



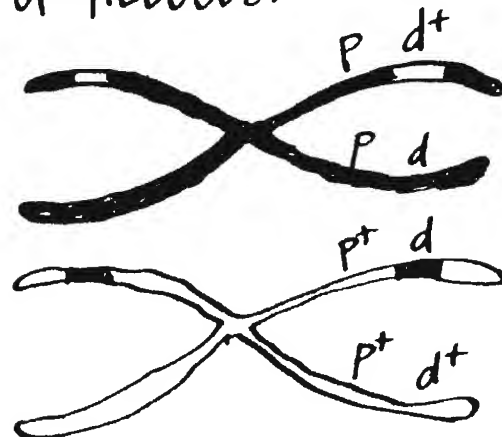
AT CERTAIN POINTS, SEEMINGLY "CHOSEN" AT RANDOM, THE CHROMOSOMES TOUCH:



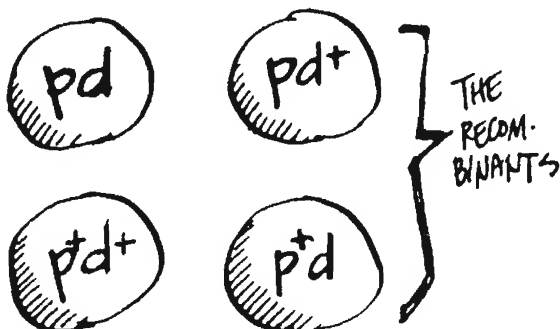
SOME SEGMENTS CROSS OVER:



WHEN THEY SEPARATE, THEY HAVE NEW COMBINATIONS OF ALLELES.



WHEN THAT HAPPENS TO OUR HETEROZYGOTE, SOME OF THE RESULTING GAMETES GET THE "RECOMBINANT" CHROMOSOMES. HENCE THE EXCEPTIONAL CROSSES!



NOTE: THANKS TO CROSSING OVER, THE CHROMOSOMES YOU PASS ALONG TO YOUR OFFSPRING ARE NOT EXACTLY YOUR OWN, BUT RATHER A SHUFFLED TOGETHER COMBINATION!

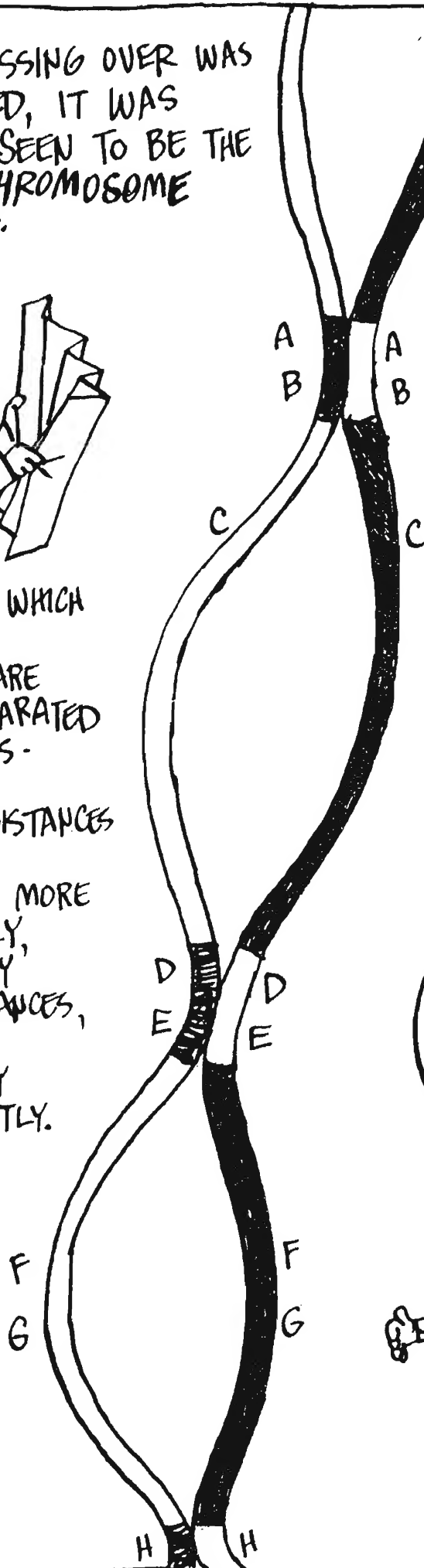


ONCE CROSSING OVER WAS DISCOVERED, IT WAS QUICKLY SEEN TO BE THE KEY TO CHROMOSOME MAPPING.

GRR-A-R



TWO GENES WHICH ARE CLOSE TOGETHER ARE RARELY SEPARATED BY A CROSS-OVER. AT GREATER DISTANCES THEY ARE SEPARATED MORE FREQUENTLY, AND AT VERY GREAT DISTANCES, THEY ACT COMPLETELY INDEPENDENTLY.



THAT IS, CROSSING OVER FREQUENCY INCREASES WITH DISTANCE!



SO HERE'S HOW YOU MAKE A GENE MAP WITHOUT EVER SEEING A SINGLE GENE:

FIRST MAKE A VAST NUMBER OF CROSSES BETWEEN INDIVIDUALS DIFFERING IN VARIOUS PAIRS OF TRAITS...

YOU'RE SOME TOMATO!



	A	B	C	D	E	F	G	H
A	0	.27	.03	.04	.33	.48	.19	.41
B	.27	0	.24	.31	.36	.45	.16	.44
C	.03	.24	0	.07	.30			
D	.04	.31	.07	0				
E	.33	.36	.30		0			
F	.48	.45				0		
G	.19	.16					0	
H	.41	.44						0

NEXT, SEE HOW OFTEN EACH PAIR IS SEPARATED BY CROSSING OVER (BY LOOKING AT THE OFFSPRING).

THEN PLOT THEM OUT: THOSE MOST CLOSELY LINKED WILL BE CLOSEST TOGETHER, ETC!

I'VE BEEN MAPPED!

F B D A C G E H

SINCE 1913, MAPPING HAS BEEN APPLIED TO A VARIETY OF ORGANISMS. NEARLY 1000 GENES HAVE BEEN MAPPED IN THE BACTERIUM *E. COLI*; ABOUT 300 IN THE TOMATO; 200 IN THE HOUSE MOUSE...; AND A FEW HUNDRED IN HUMAN BEINGS, ALTHOUGH THIS WAS DONE BY DIFFERENT MEANS...

WHY THE DIFFERENCE FOR HUMANS?

THEY WON'T LET US DO BREEDING EXPERIMENTS...



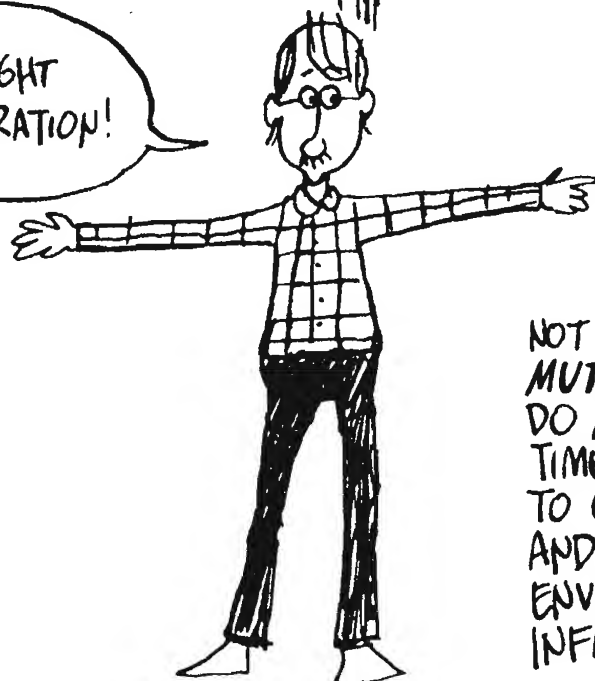
MUTATION, OR

A CHANGE OF GENES



SO FAR, WE HAVE BEEN
THINKING OF GENES AS
"ATOMS OF INHERITANCE"—
UNCHANGING, IMMUTABLE
UNITS OF HEREDITY.

A SLIGHT
EXAGGERATION!

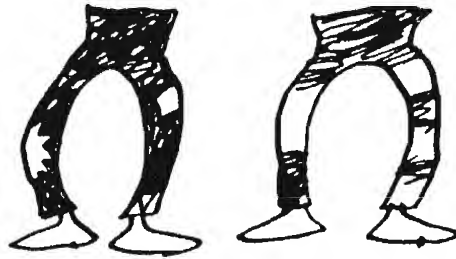


NOT ONLY ARE GENES
MUTABLE, BUT THEY
DO MUTATE FROM
TIME TO TIME, OWING
TO COPYING ERRORS
AND VARIOUS
ENVIRONMENTAL
INFLUENCES.

THESE MUTATIONS - IT MEANS "CHANGES" IN LATIN - ARE FAIRLY RARE: THE CHANCE OF FINDING A MUTATION IN A GIVEN GENE IN AN INDIVIDUAL IS

THOUGH SOME GENES ARE MORE PRONE TO CHANGE THAN OTHERS!

→ 1 IN 100,000



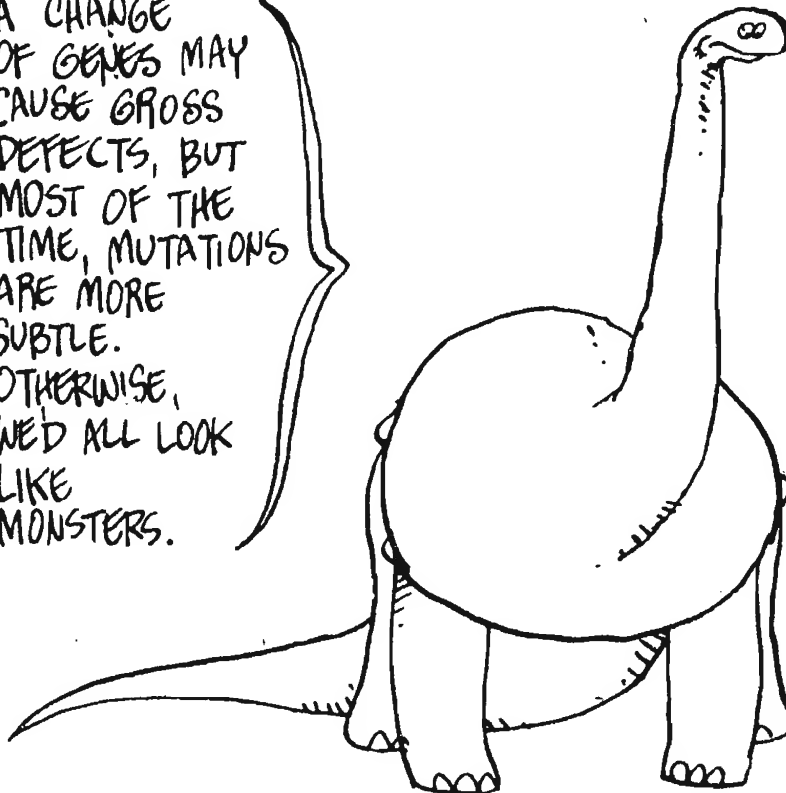
EVEN AT THIS RATE, THEY DO ADD UP! A HUMAN HAS SOME 200,000 GENES, SO WE CARRY AN AVERAGE OF TWO NEW MUTATIONS A PIECE.

GREAT SHADES!



SORRY... THOSE ARE MY EYES...

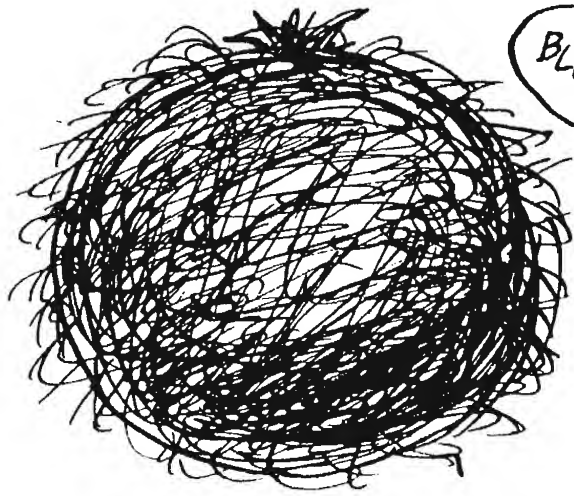
A CHANGE OF GENES MAY CAUSE GROSS DEFECTS, BUT MOST OF THE TIME, MUTATIONS ARE MORE SUBTLE. OTHERWISE, WE'D ALL LOOK LIKE MONSTERS.



SAY - YOU DON'T LOOK THAT GREAT!



SOMETIMES, MUTATIONS MERELY RESULT IN A NEW **RECESSIVE ALLELE**, LIKE HAIRINESS IN TOMATOES. YOU DON'T SEE ANYTHING AT ALL UNTIL TWO INDIVIDUALS WITH THE SAME MUTATION MATE TO FORM A **HOMOZYGOTE**. THEN _____



BLEUGH!

SOMETIMES MUTATIONS ARE COMPLETELY SILENT — PRODUCING NO CHANGE AT ALL — AND SOMETIMES THEY CAUSE CHANGES SO SLIGHT AS TO BE BARELY PERCEPTIBLE....



LIKE AN EXTRA MILLIMETER ON THE NOSE!

BUT EVERY SO OFTEN THE GENETIC "ERROR" MAY BE OF POSITIVE ADVANTAGE TO THE LUCKY MUTANT!!



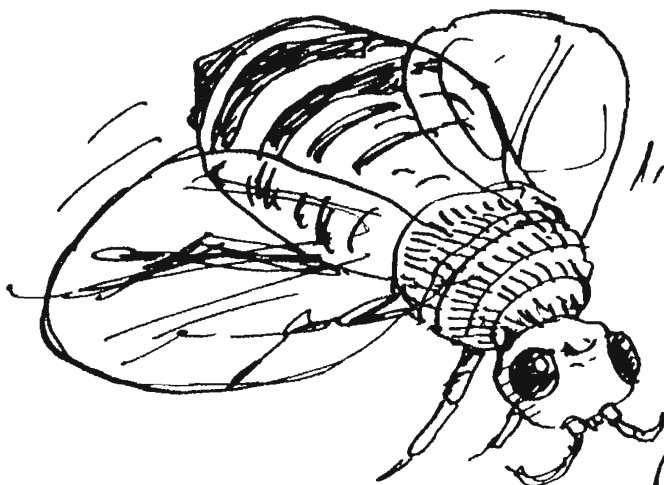
HM! SO THE EGG DID COME BEFORE THE CHICKEN!



MUTATIONS ARE NOT ALWAYS SPONTANEOUS... FAR FROM IT... ALL SORTS OF OUTSIDE INFLUENCES CAN INCREASE THE NORMAL FREQUENCY OF MUTATION... SUCH AGENTS ARE CALLED MUTAGENS.

SOME CHEMICALS ARE MUTAGENS...

SO IS MOST RADIATION... HERMANN MÜLLER WAS THE FIRST TO DEMONSTRATE THE MUTAGENIC POWER OF X-RAYS, IN 1927, WHEN HE IRRADIATED FRUIT FLIES (A FAVORITE ANIMAL OF GENETICISTS).



QUICKLY HERMANN!! LOWER THE DOSE!

EH?



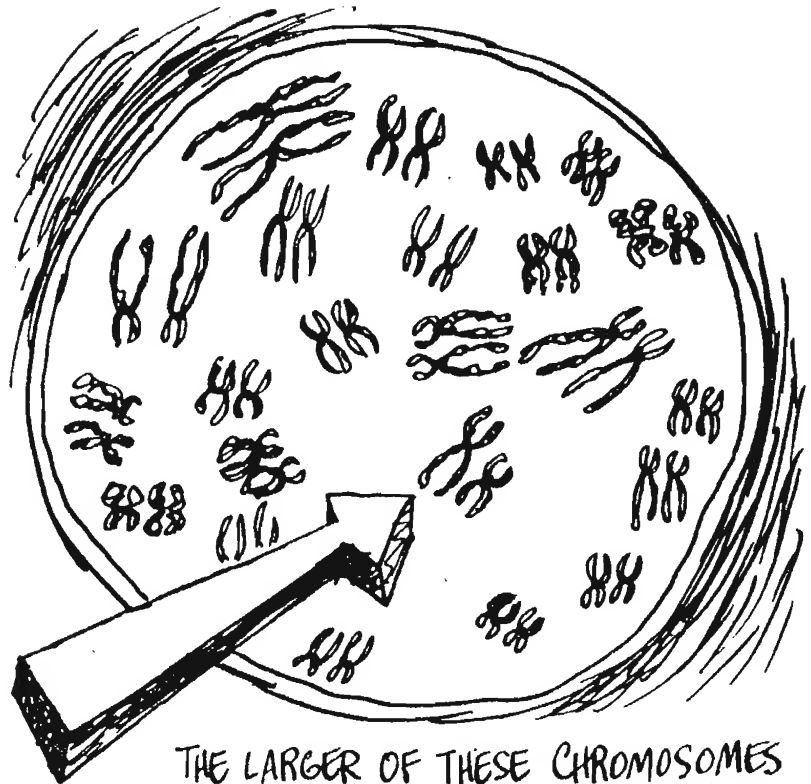


MUTATION IN BODY CELLS (SOMATIC CELLS, AS DISTINCT FROM GERM CELLS) MAY BE INVOLVED IN CANCER... IT MAKES SENSE: THE GENES CONTROL EVERYTHING ABOUT THE CELL, INCLUDING THE PROCESS OF DIVISION. ALTHOUGH THERE ARE STILL MANY MYSTERIES ABOUT CANCER, IT INVOLVES MUTATIONS THAT LEAD THE CELL TO DIVIDE OUT OF CONTROL.

MANY MUTAGENIC AGENTS ARE ALSO CARCINOGENIC (CANCER-CAUSING) — WHICH IS WHY THE FOOD + DRUG PEOPLE LOOK OUT FOR MUTAGENIC FOOD ADDITIVES... AND WHY YOU SHOULD LIMIT YOUR SUNBATHING, ESPECIALLY IF YOU HAVE PALE SKIN. (ULTRAVIOLET LIGHT IS MUTAGENIC.)



BUT OF COURSE IT'S
IN THE GENES...
NOT LONG AFTER
HOMOLOGOUS
CHROMOSOMES WERE
DISCOVERED,
SOMEBODY NOTICED
AN EXCEPTION:
HUMAN MALES HAVE
ONE PAIR THAT IS
NOT HOMOLOGOUS!!



THE LARGER OF THESE CHROMOSOMES
WAS CALLED X; THE SMALLER, Y.

THE ONLY GENETIC DIFFERENCE BETWEEN (HUMAN) MALES AND
FEMALES IS THIS:

FEMALES
HAVE
TWO
X
CHROMOSOMES:

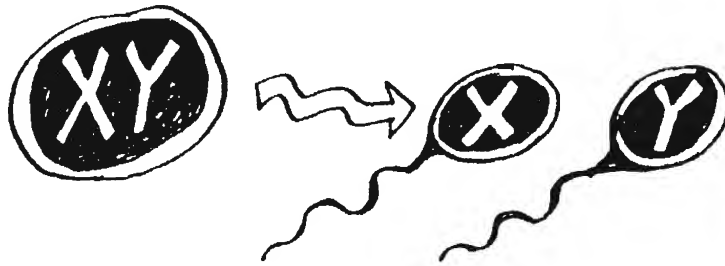
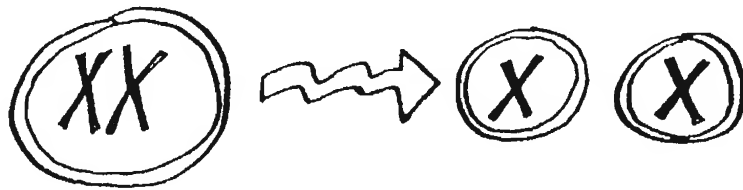


WHILE
MALES
HAVE ONE
X AND
ONE Y:

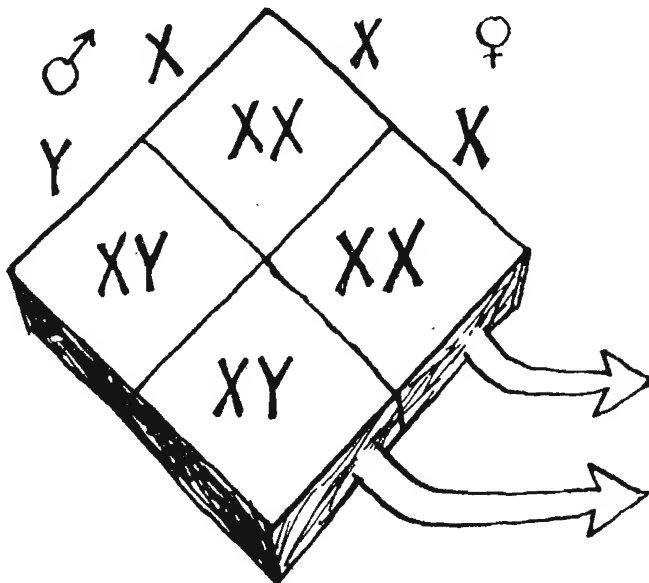


THE OTHER 22 OTHER PAIRS OF CHROMOSOMES ARE THE SAME.

LET'S JUST MAKE
SURE THIS PRODUCES
BOY AND GIRL
BABIES IN THE
RIGHT AMOUNTS.



MEIOSIS PRODUCES EGGS CARRYING THE X CHROMOSOME; SPERM
ARE EQUALLY DIVIDED BETWEEN X AND Y —



SO:

$\frac{1}{2}$ GIRLS

$\frac{1}{2}$ BOYS



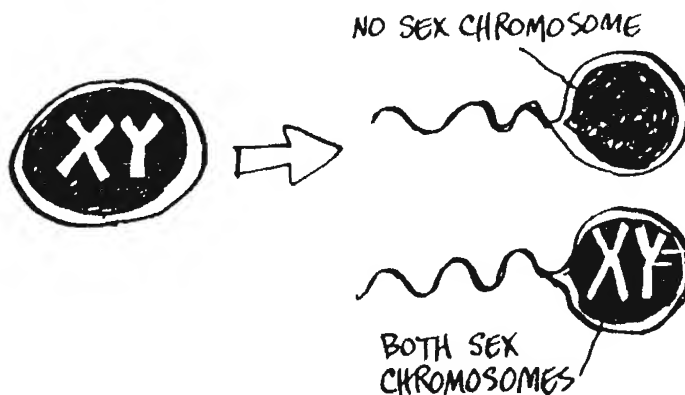
HOWEVER, THE BASIC GENETIC QUESTION REMAINS: WHICH GENES ARE RESPONSIBLE FOR WHAT? IS IT THE Y CHROMOSOME THAT MAKES A MALE, OR DOES IT TAKE A DOUBLE DOSE OF X TO MAKE A FEMALE? WHAT WOULD HAPPEN TO SOMEBODY WITH TWO X CHROMOSOMES AND A Y ??



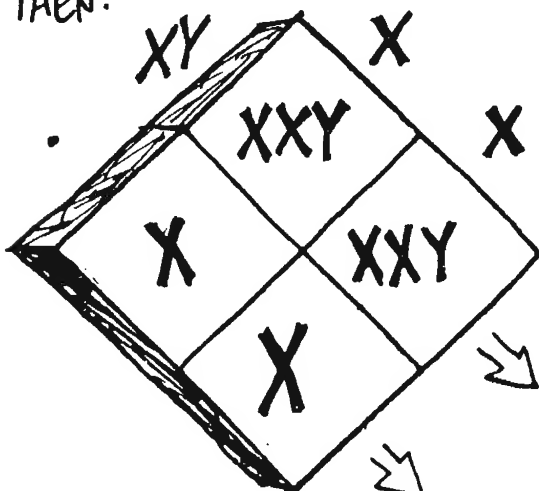
THIS ACTUALLY HAPPENS !!



THESE QUESTIONS ARE ANSWERED BY LOOKING AT CASES OF FAULTY MEIOSIS... SOMETIMES THERE IS AN ERROR IN MAKING SPERM:



THEN:



"KLEINFELTER'S SYNDROME"
"TURNER'S SYNDROME"

THE XXY ("KLEINFELTER'S SYNDROME") GROWS UP MALE. EVEN IN THE PRESENCE OF TWO X CHROMOSOMES, THE Y CAUSES MALENESS. THE SINGLE X GROWS UP FEMALE.

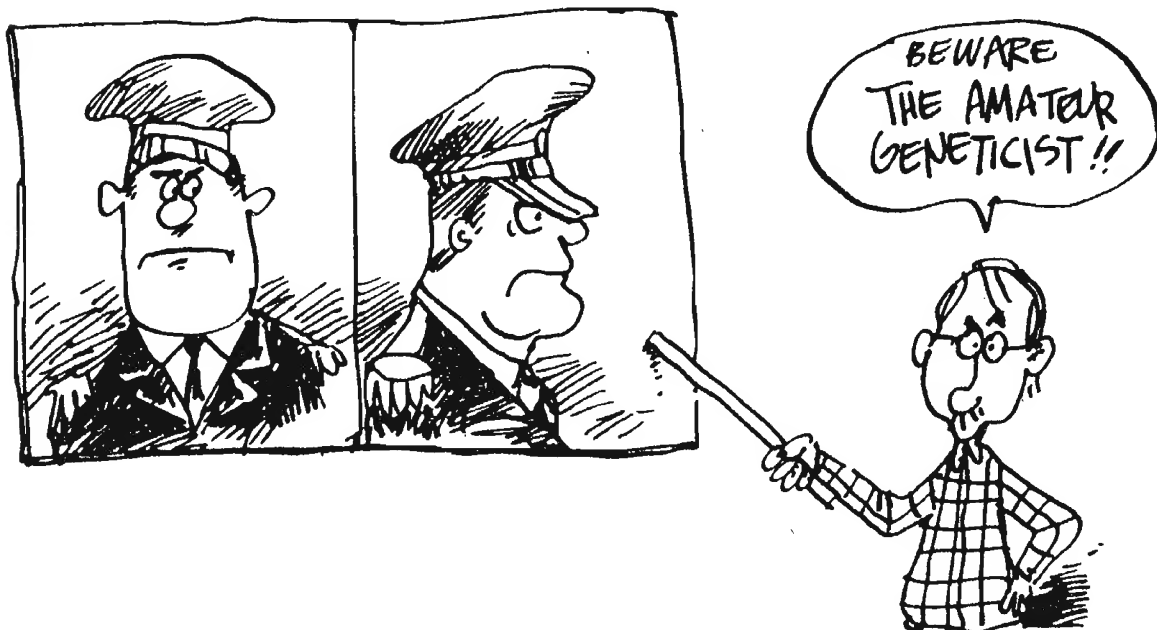


ANOTHER ABNORMALITY IS THE "SUPER MALE" COMBINATION XYY , WHICH OCCURS IN ABOUT ONE BIRTH IN A THOUSAND. XYY CHILDREN GROW UP TO BE NORMAL MALES — EXCEPT THAT THEY END UP IN PRISON ABOUT 20 TIMES MORE OFTEN THAN THE REST OF THE POPULATION. ABOUT 5% OF ALL PRISONERS HAVE AN EXTRA Y CHROMOSOME. SOME SAY:



*KARYOTYPE = AN ORGANISM'S PATTERN OF CHROMOSOMES

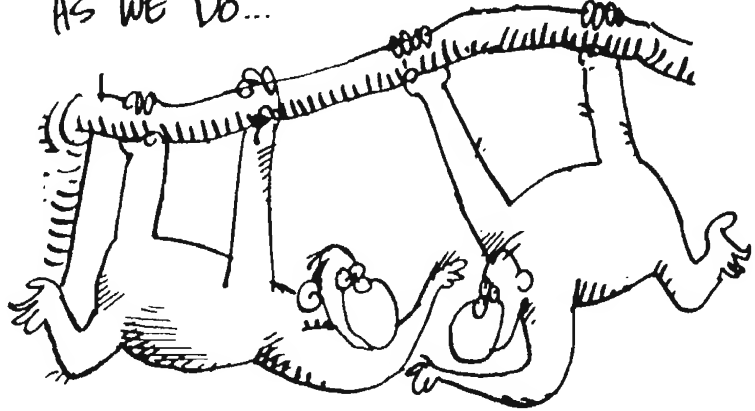
MOST GENETICISTS WOULD BE MORE CAUTIOUS.. THE VAST MAJORITY (OVER 95 %) OF XYY MALES ARE NOT IN PRISON... SO IT'S IMPOSSIBLE TO SAY THAT THE XYY KARYOTYPE CAUSES CRIMINALITY!



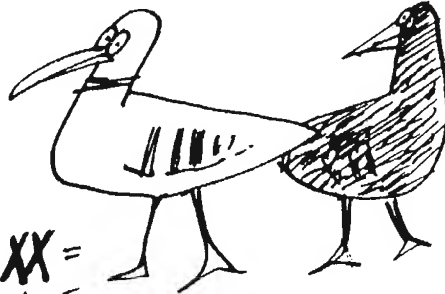
DO ANIMALS
DO IT WITH
X'S AND Y'S?



NOT NECESSARILY. SEX DETERMINATION IS HANDLED ALL SORTS OF WAYS, THOUGH MANY, MANY SPECIES HAVE THE SAME SYSTEM AS WE DO...



BUT AMONG BIRDS IT'S JUST THE OPPOSITE —



AND BEES ARE REALLY BEE-ZARRE: MALES DEVELOP FROM UNFERTILIZED EGGS. THEY'RE ALL HAPLOID, WHEREAS ALL DIPLOIDS ARE FEMALE (THE VAST MAJORITY OF THE HIVE). OTHERWISE, BEES HAVE NO SPECIFIC SEX CHROMOSOMES.

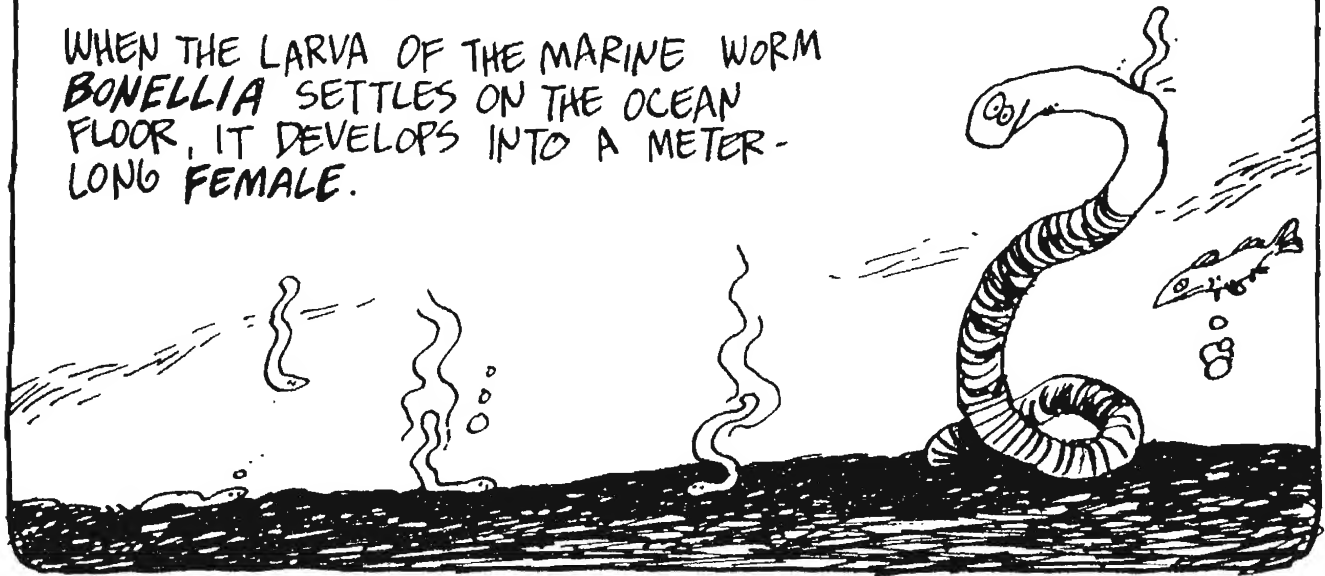
WILL YOU LISTEN
TO ME? I SWEAR,
BUSTER, IT'S LIKE
YOU'RE ONLY HALF
THERE SOMETIMES!

HUH?

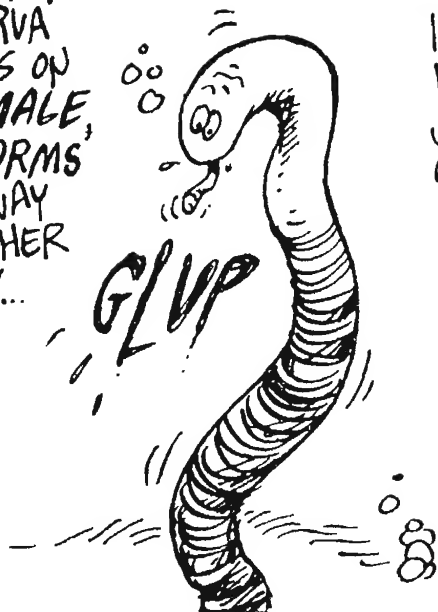


THEN THERE ARE THE TRUE ODDITIES, WITH NO GENETIC DIFFERENCE BETWEEN MALE AND FEMALE AT ALL...

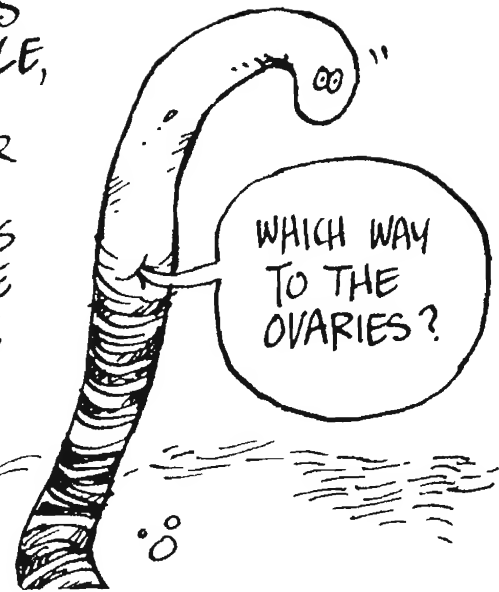
WHEN THE LARVA OF THE MARINE WORM **BONELLIA** SETTLES ON THE OCEAN FLOOR, IT DEVELOPS INTO A METER-LONG FEMALE.



BUT WHEN A LARVA LANDS ON A FEMALE, IT WORMS ITS WAY INTO HER BODY...



...IN WHICH CASE, IT MATURES INTO A MALE, JUST A CENTIMETER LONG, AND PASSES ITS WHOLE LIFE INSIDE THE FEMALE!



AND SOMETIMES SEXUAL DIFFERENCES ARE SIMPLY SUBTLE... CERTAIN PROTOZOA HAVE TWO SEXES, BUT THEY DIFFER ONLY IN A SINGLE GENE... THESE ORGANISMS USUALLY REPRODUCE ASEXUALLY, AS FINDING AN APPROPRIATE PARTNER MUST NOT BE EASY!



EXCUSE ME — ARE YOU ANY DIFFERENT FROM ME?

IF YOU CAN'T TELL, HOW CAN I?



X-RATED GENES

NOW BACK TO HUMANS...
WE'VE SEEN THAT ALL
THE GENES ACCOUNTING FOR
PURELY SEX-RELATED MATTERS
HAVE ACCUMULATED ON JUST
TWO CHROMOSOMES, X FOR
FEMALE, Y FOR MALE...



NOW WE MIGHT ASK THE FOLLOWING

QUESTION:

ARE THERE ANY
OTHER GENES
ON THESE CHROMO-
SOMES ????

THERE'S A GOOD REASON TO ASK: HUMANS EXHIBIT SEVERAL
DEFECTS THAT APPEAR TO BE SEX-LINKED...

MOST BALD
PEOPLE
ARE MEN.



SO ARE
MOST
COLOR-
BLIND
PEOPLE.

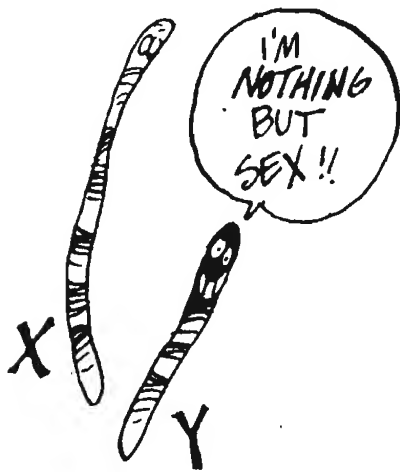


DITTO
FOR
Hemo-
PHILIACS.*



*HEMOPHILIA = A FAILURE OF THE BLOOD TO CLOT. HEMOPHILIACS CAN BLEED TO DEATH FROM A SMALL CUT.

FROM THIS YOU MIGHT CONCLUDE THAT THESE GENES LIE ON THE Y CHROMOSOME— BUT YOU'D BE WRONG!! ACTUALLY, HEMOPHILIA, COLOR-BLINDNESS, AND HEREDITARY BALDNESS ARE ALL CAUSED BY **RECESSIVE ALLELES** LYING ON THE **X CHROMOSOME!!**



TAKE THE EXAMPLE OF BALDNESS:



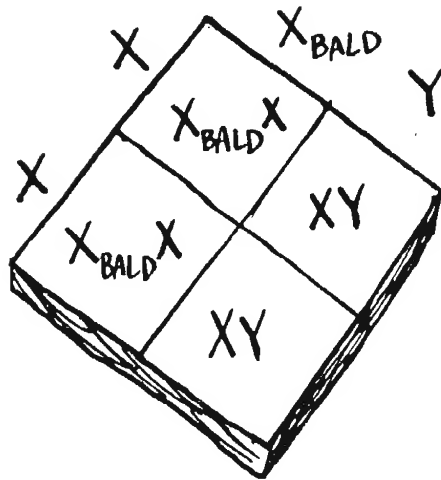
THE REASON WOMEN ARE RARELY BALD IS THAT, EVEN IF THEY HAVE THE BALDNESS ALLELE ON ONE X CHROMOSOME, THEY USUALLY HAVE THE DOMINANT NON-BALD ON THE OTHER.



BUT IT SHOWS UP IN MEN BECAUSE THE Y CHROMOSOME HAS NO ALLELE FOR THAT GENE AT ALL. IN THE ABSENCE OF A DOMINANT ALLELE, THE RECESSIVE IS EXPRESSED!!

LET'S SEE HOW THESE SEX-LINKED GENES ARE PASSED ALONG:

SUPPOSE A
NORMAL WOMAN
(XX) HAS
CHILDREN BY
A BALD MAN
($X_{BALD}Y$).

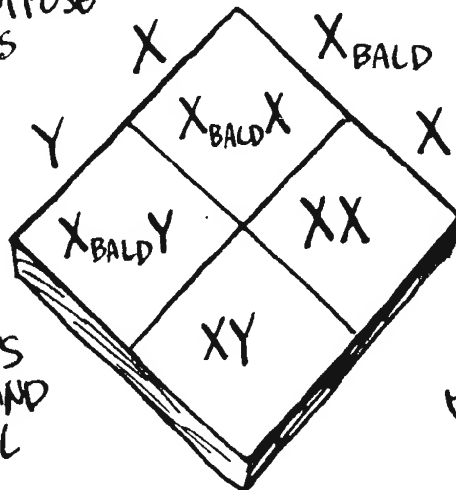


THE DAUGHTERS ($X_{BALD}X$)
ARE ALL CARRIERS.... NOT
BALD THEMSELVES, THEY STILL
CARRY THE RECESSIVE GENE.
THE SONS ARE NORMAL.

IF YOUR MOTHER IS
NORMAL, YOU CAN'T
INHERIT BALDNESS
FROM YOUR FATHER!



NEXT GENERATION: SUPPOSE
ONE OF THE CARRIERS
MARRIES A
NORMAL MAN.



ON THE AVERAGE,
HALF THE DAUGHTERS
WILL BE CARRIERS, AND
HALF THE SONS WILL
BE BALD!

YOU CAN INHERIT
BALDNESS FROM
YOUR MATERNAL
GRANDFATHER!!



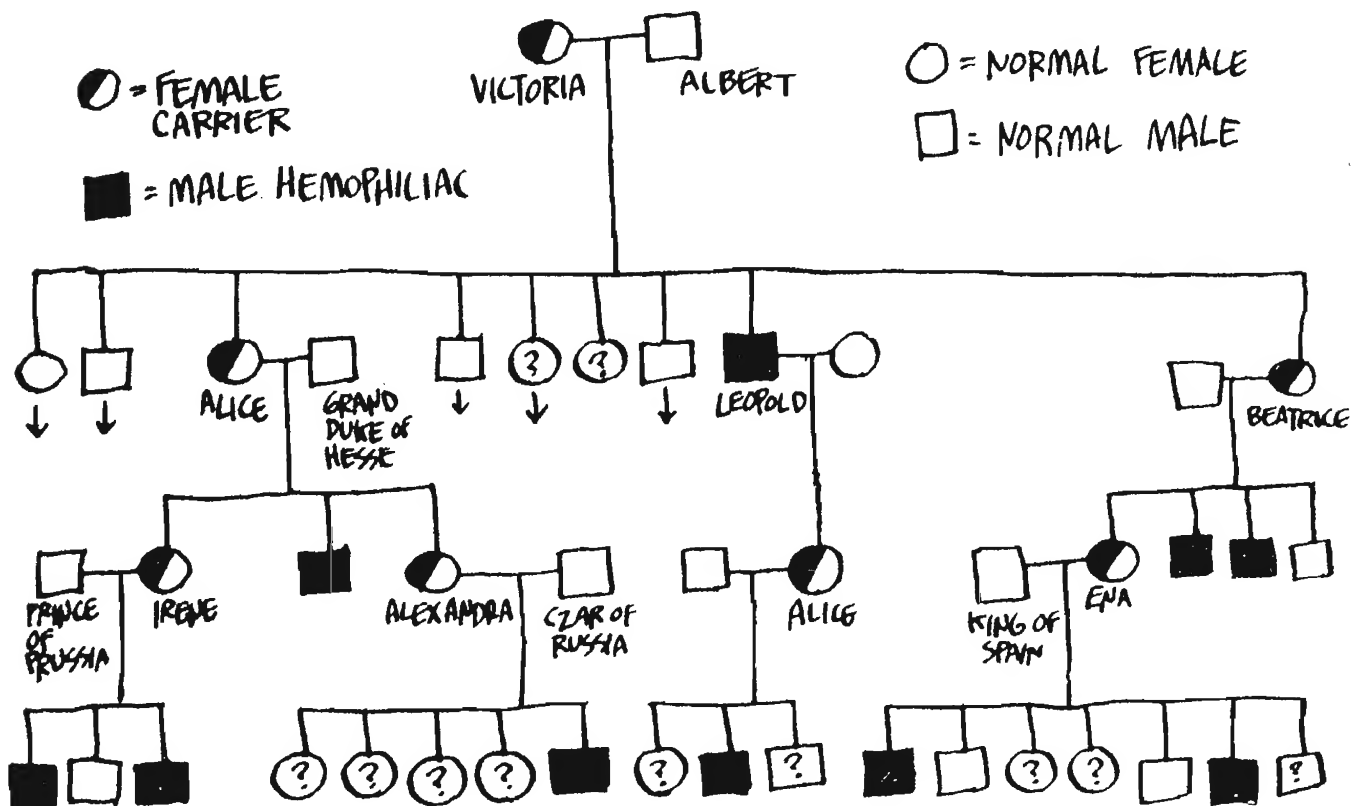


HEMOPHILIA FOLLOWS
THE SAME PATTERN.
THE MOST FAMOUS EXAMPLE
WAS QUEEN VICTORIA
OF ENGLAND, WHO
WAS A CARRIER.

THERE IS NO RECORD OF HEMOPHILIA IN VICTORIA'S
ANCESTORS, SO WE MAY ASSUME THE DEFECT APPEARED
IN HER GENES AS A SPONTANEOUS MUTATION. THIS HAPPENS
WITH HEMOPHILIA IN AN ESTIMATED 1 CASE IN EVERY
50,000 PARENTS.



HEMOPHILIA IS PASSED ALONG JUST LIKE BALDNESS, AND YOU CAN SEE THE PATTERN IN VICTORIA'S FAMILY TREE



VICTORIA'S NUMEROUS BROOD INTERMARRIED WITH THE ROYAL HOUSES OF EUROPE, SPREADING THEIR MEDICAL PROBLEMS INTO PRUSSIA, SPAIN, AND PRE-REVOLUTIONARY RUSSIA...



WELL

JUST LOOK HOW FAR SCIENCE HAD COME BY THE EARLY 19TH CENTURY: MENDEL AND HIS HEIRS HAD POLISHED OFF ALL THOSE OLD PUZZLES: THE ROLE OF MOTHER AND FATHER, THE NATURE OF HYBRIDS AND "SPORTS," WHAT DETERMINES SEX, AND EVEN WHAT CAUSES THE QUALITIES OF LIVING THINGS...

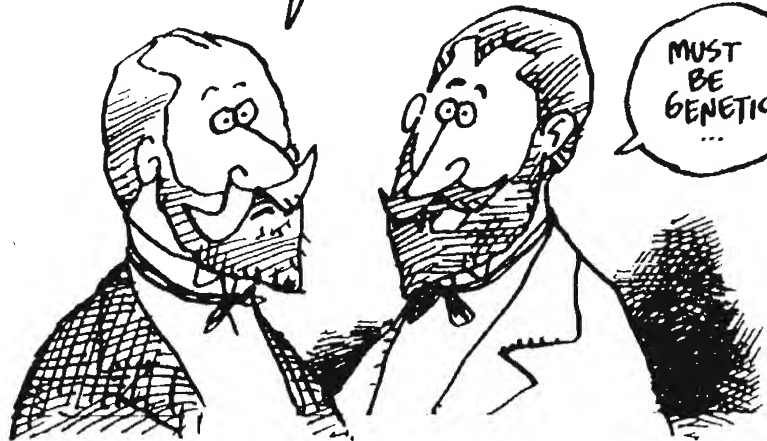


ALL THESE HAD BEEN EXPLAINED IN TERMS OF **GENES**...

GENES HAD BEEN LOCATED, MAPPED, AND THEIR PATTERNS OF INHERITANCE ANALYZED. NOW JUST ONE QUESTION REMAINED ~.

YES - WHY DO GENETICISTS WEAR POINTED BEARDS??

MUST BE GENETIC ...



NO - THE QUESTION IS: WHAT ARE THE GENES, AND HOW DO THEY WORK??



GET READY TO TRAVEL TO UNEXPLORED TERRITORY!

WHAT'S IN A CELL?

HERE WE SEE A
COUPLE OF TYPICAL
LIFE FORMS: A
GORILLA AND A
BANANA... THE
QUESTION IS --

HOW DO THE **GENES**
WORK TO MAKE THE
GORILLA A GORILLA
AND THE BANANA A
BANANA... ??



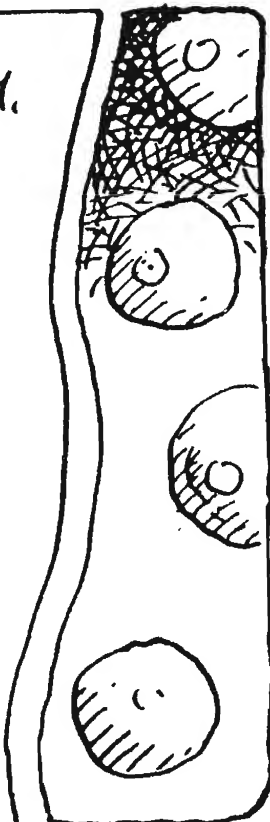
LET'S TAKE
A CLOSER
LOOK!



FROM HERE YOU CAN SEE
HOW THE GORILLA IS
MADE OF CELLS. TO
UNDERSTAND THE APE,
WE'LL HAVE TO MAKE SENSE
OF WHAT GOES ON IN THESE
TINY CHEMICAL FACTORIES.



UNFORTUNATELY,
NOT ALL
GORILLA
CELLS ARE
ALIKE...
THESE RED
BLOOD CELLS
ARE DIFFERENT
FROM SKIN
CELLS IN
SEVERAL
WAYS...

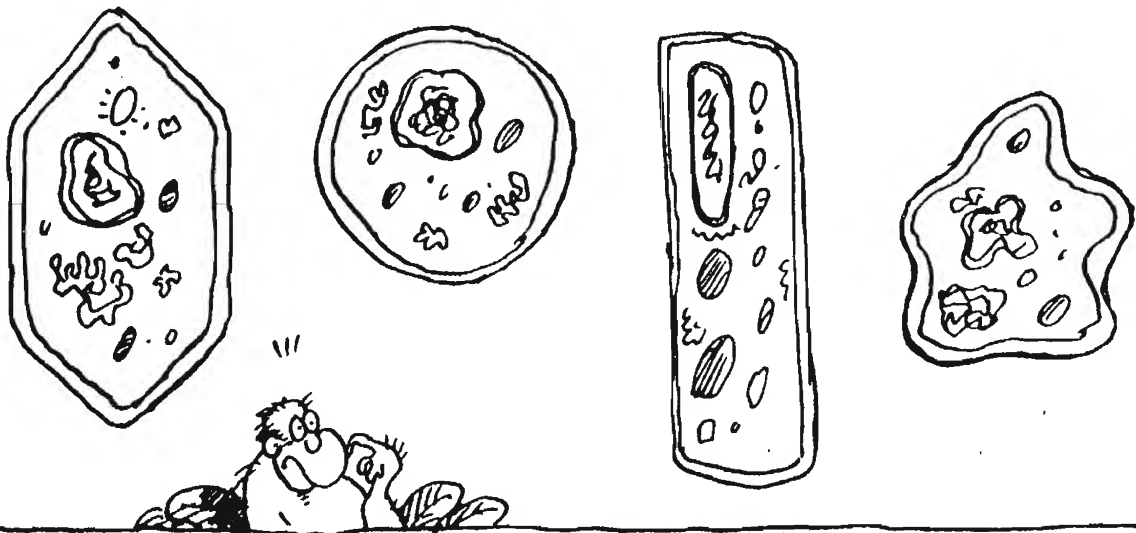


NERVE
CELLS
ARE
LONG
AND
SKINNY
...2



AND THE
CELLS
OF
MUSCLES,
EYES,
KIDNEYS,
ETC
ETC
ETC
...
ALL
DIFFERENT
!!!

SIMILARLY, THE BANANA PRESENTS A WIDE DIVERSITY OF CELL TYPES...

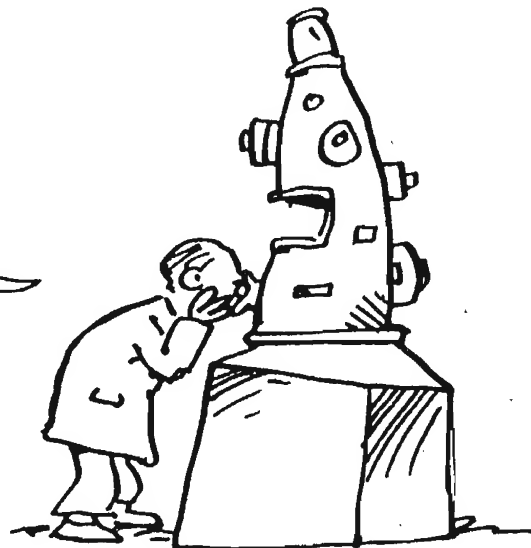


...EACH OF WHICH IS FILLED WITH ALL SORTS OF EVEN TINNER BODIES...



... MAKING BANANAS AND GORILLAS EXTREMELY HARD TO FIGURE OUT !!

HMM... THE GOLGI BODY CONNECTED TO THE ENDOPLASMIC RETICULUM... THE ENDOPLASMIC RETICULUM CONNECTED TO THE NUCLEAR MEMBRANE... NUCLEAR MEMBRANE CONNECTED TO...
SIGH



WHY DIDN'T I
LISTEN TO MY MAMA
AND BECOME A
LAWYER?



IN FACT, GORILLAS AND
BANANAS ARE SO
COMPLICATED, THAT
FOR MANY YEARS
SCIENTISTS DESPAIRED
OF EVER UNDER-
STANDING THE
MOLECULAR GENETICS
OF PLANTS AND
ANIMALS.

INSTEAD, THEY
STUDIED A MUCH
SIMPLER ORGANISM:
A TINY CREATURE
FOUND LIVING BY
THE BILLION —
RIGHT...IN... HERE!!



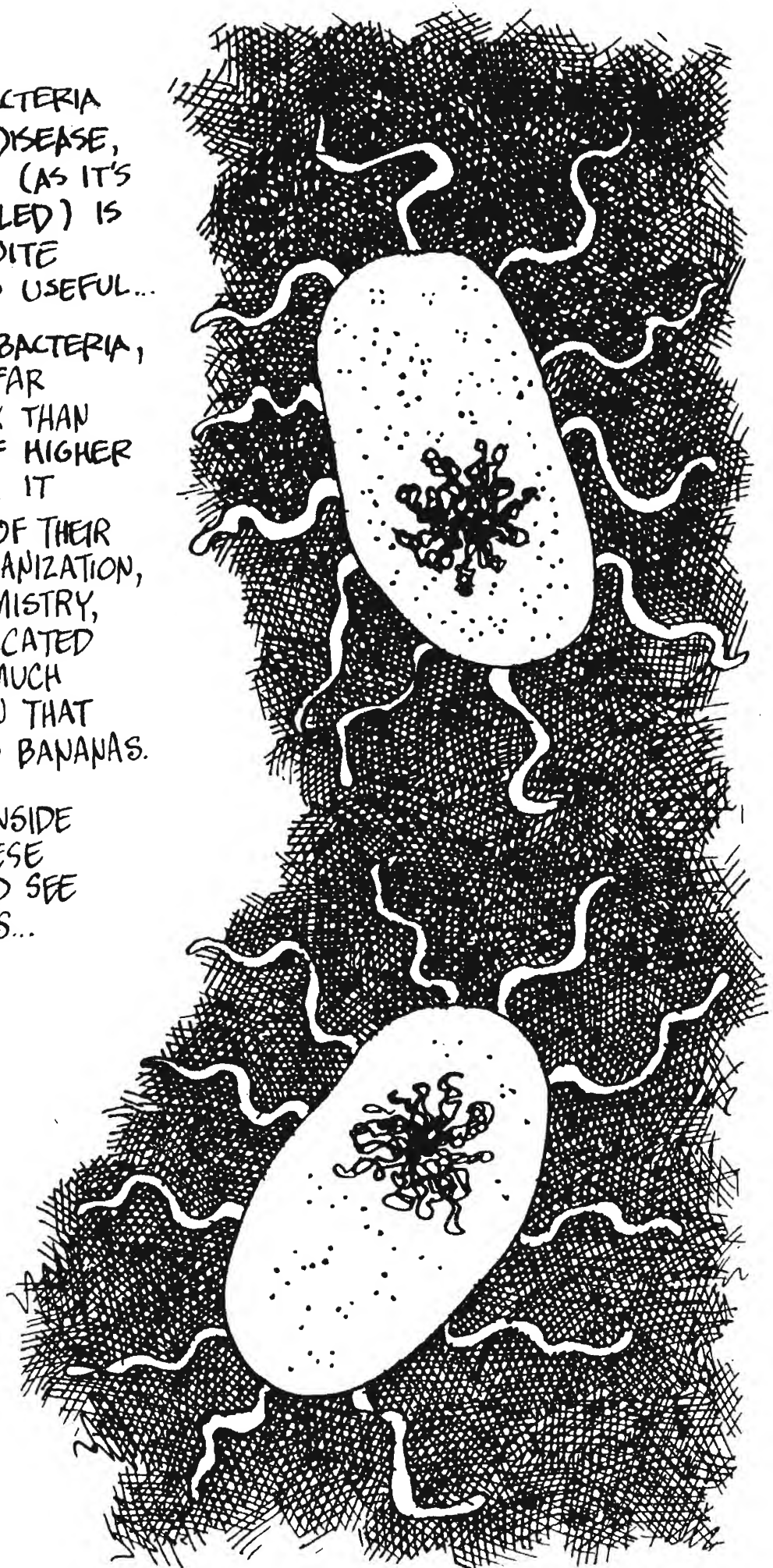
THIS IS THE
BACTERIUM,
ESCHERECHIA
COLI, THAT
THRIVES IN THE
INTESTINES OF
APES AND
HUMANS.

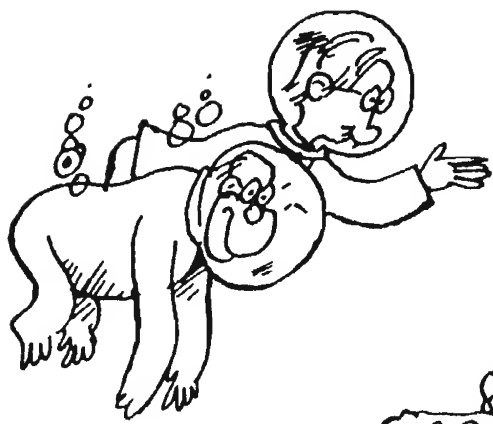


WE TEND TO
THINK OF BACTERIA
IN TERMS OF DISEASE,
BUT *E. COLI* (AS IT'S
USUALLY CALLED) IS
ACTUALLY QUITE
BENIGN AND USEFUL...

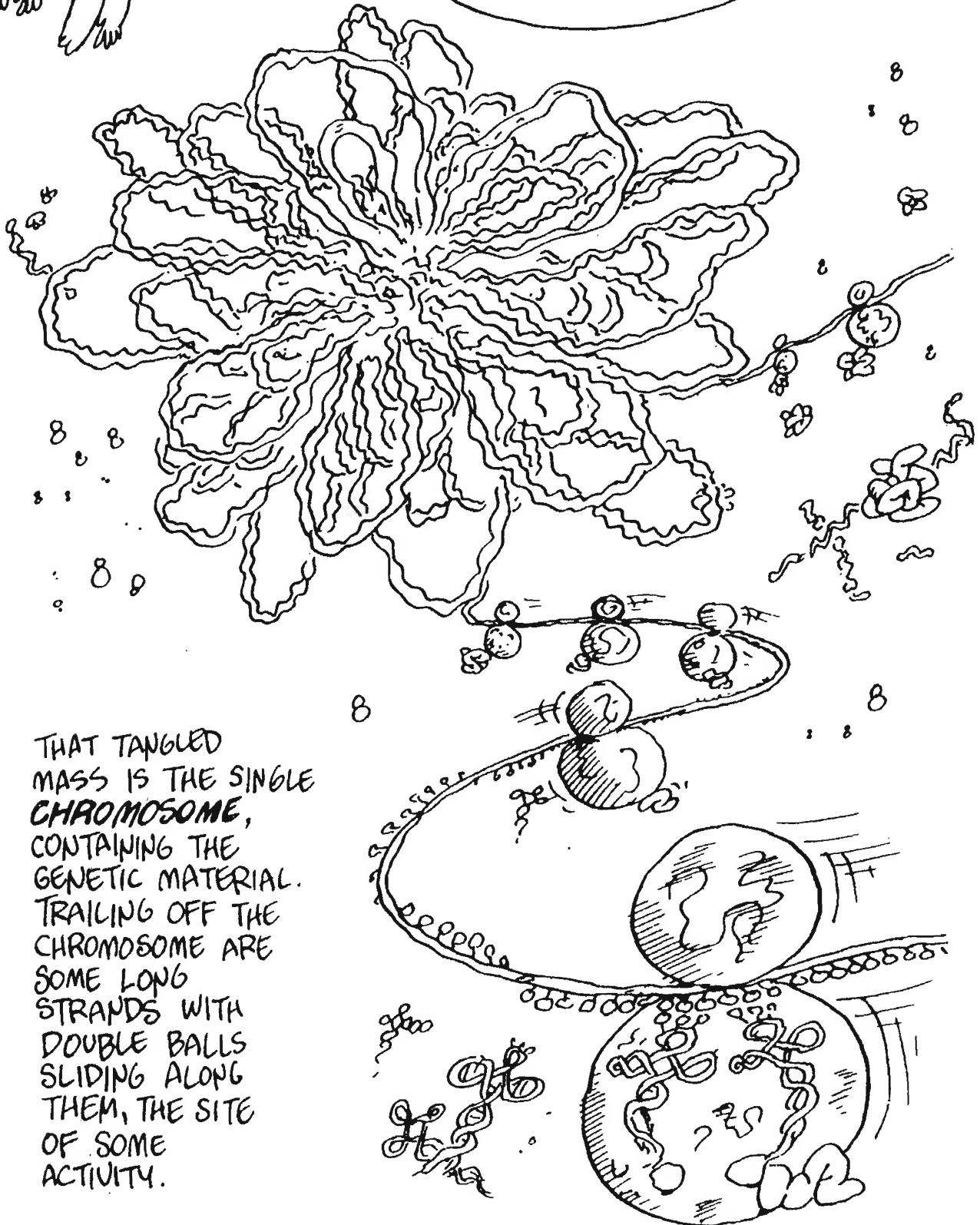
LIKE OTHER BACTERIA,
E. COLI IS FAR
LESS COMPLEX THAN
THE CELLS OF HIGHER
LIFE FORMS. IT
LACKS MOST OF THEIR
INTERNAL ORGANIZATION,
AND ITS CHEMISTRY,
WHILE COMPLICATED
ENOUGH, IS MUCH
SIMPLER THAN THAT
OF APES AND BANANAS.

LET'S GET INSIDE
ONE OF THESE
E. COLI AND SEE
HOW IT LOOKS...

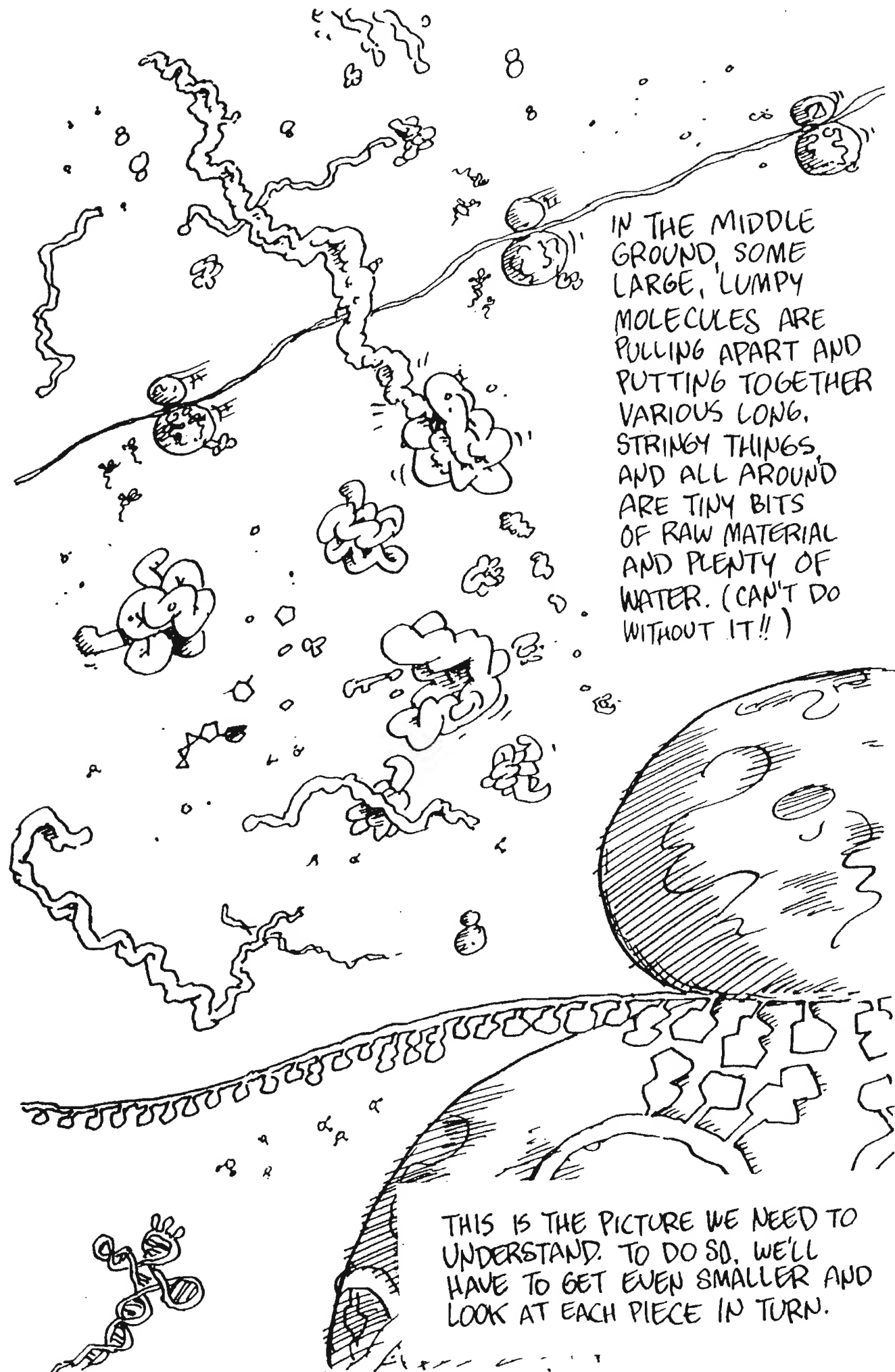




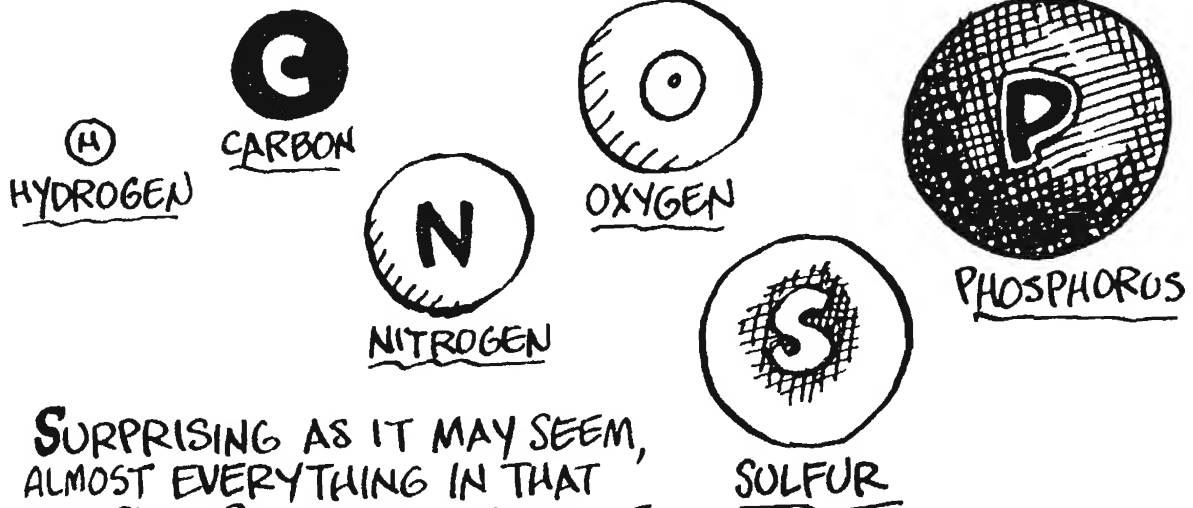
THIS IS THE VIEW
FROM INSIDE THE BACTERIUM
E. COLI !! ALTHOUGH IT
LOOKS PRETTY CONFUSING
AT FIRST, WE CAN MAKE
OUT A FEW OBVIOUS
FEATURES!



THAT TANGLED
MASS IS THE SINGLE
CHROMOSOME,
CONTAINING THE
GENETIC MATERIAL.
TRAILING OFF THE
CHROMOSOME ARE
SOME LONG
STRANDS WITH
DOUBLE BALLS
SLIDING ALONG
THEM, THE SITE
OF SOME
ACTIVITY.

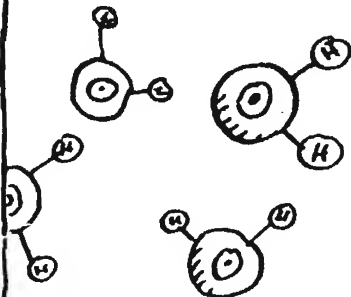


MACROMOLECULES



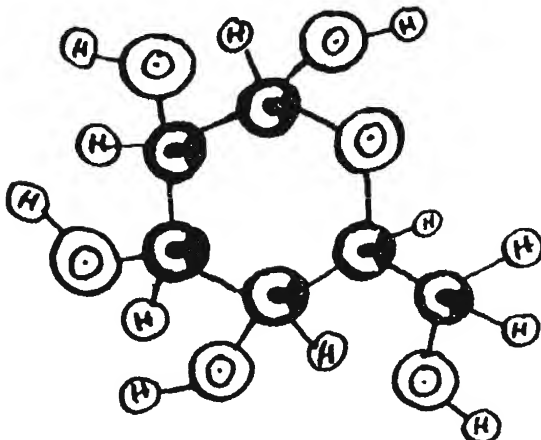
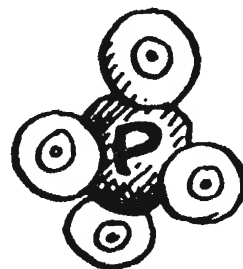
SURPRISING AS IT MAY SEEM,
ALMOST EVERYTHING IN THAT
COMPLEX PICTURE IS MADE OF
JUST SIX DIFFERENT ELEMENTS.

IN THE CELL THESE ATOMS ARE JOINED TOGETHER TO
FORM **MOLECULES**.



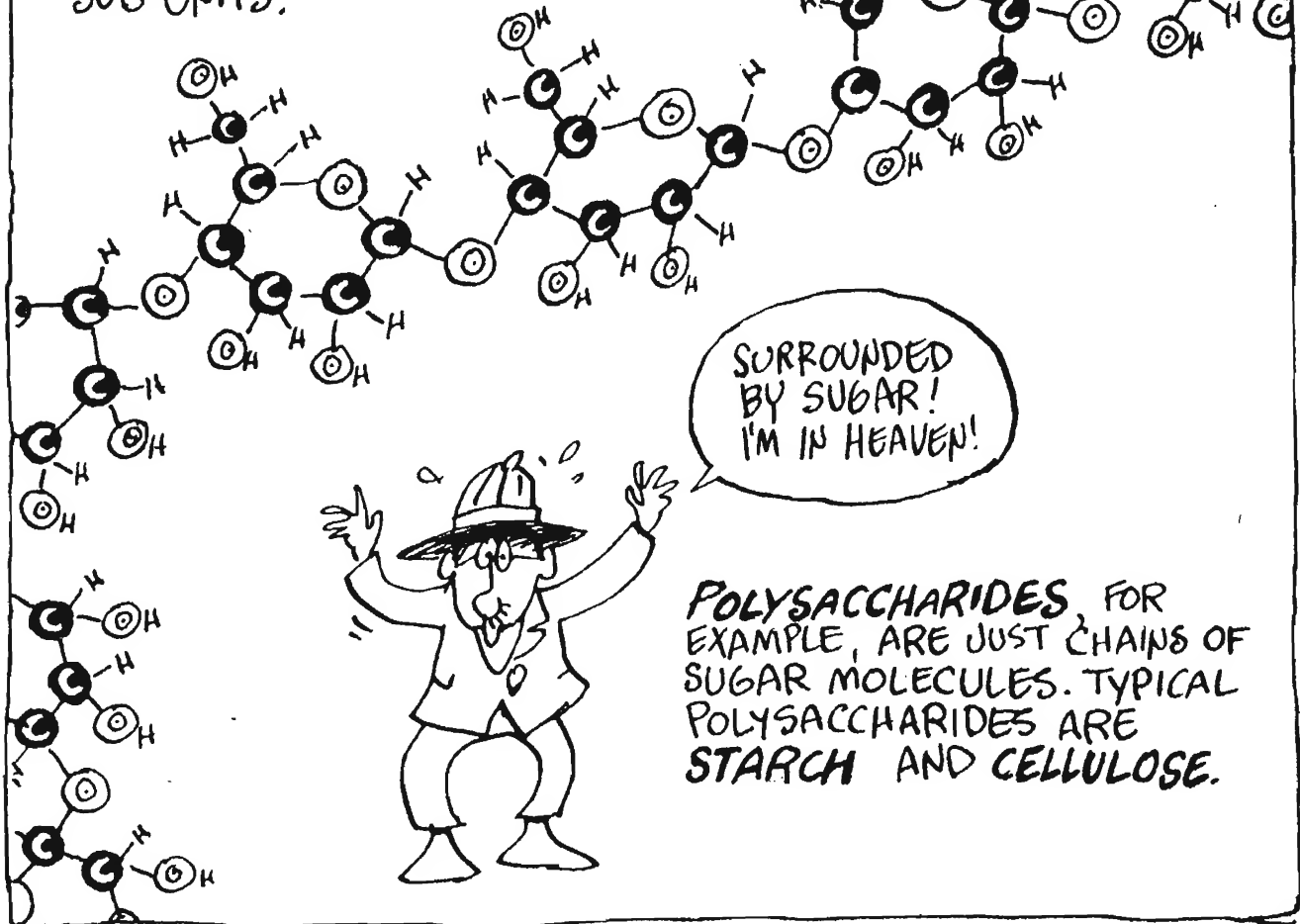
THE SIMPLEST AND MOST
ABUNDANT BY FAR IS
WATER, H_2O .

ANOTHER SMALL ONE IS
THE PYRAMID-SHAPED
PHOSPHATE, PO_4 .

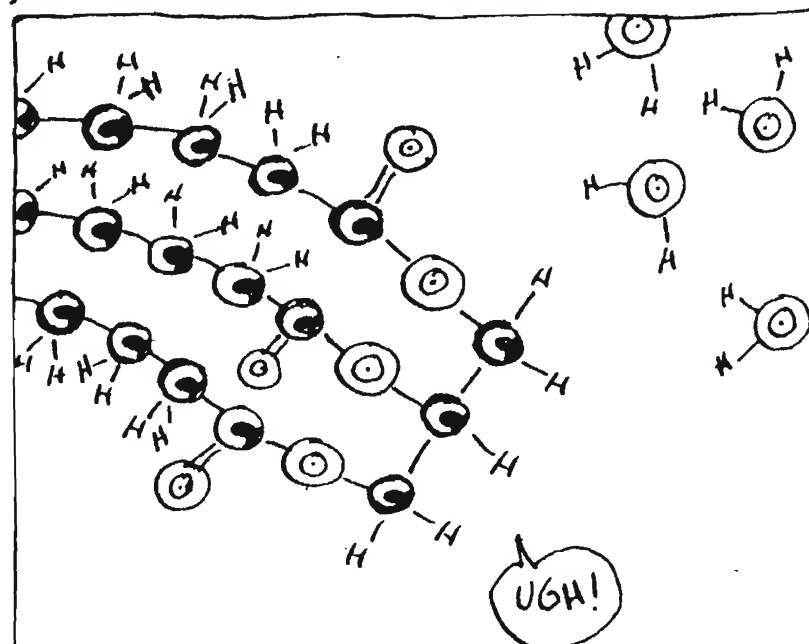


A BIT BIGGER ARE
THE RING-SHAPED
SUGARS. THIS ONE
IS **GLUCOSE**, $C_6H_{12}O_6$.

BUT MOST KINDS OF MOLECULES IN THE LIVING CELL ARE ENORMOUS, CONSISTING OF THOUSANDS OF ATOMS. THESE **MACROMOLECULES**, THOUGH LARGE, ARE GENERALLY MADE BY STRINGING TOGETHER MANY COPIES OF IDENTICAL SUB-UNITS.



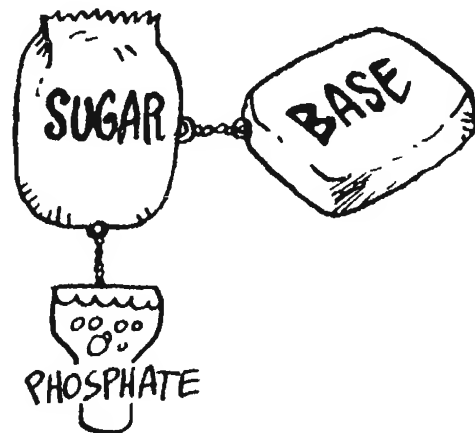
POLYSACCHARIDES, FOR EXAMPLE, ARE JUST CHAINS OF SUGAR MOLECULES. TYPICAL POLYSACCHARIDES ARE **STARCH** AND **CELLULOSE**.



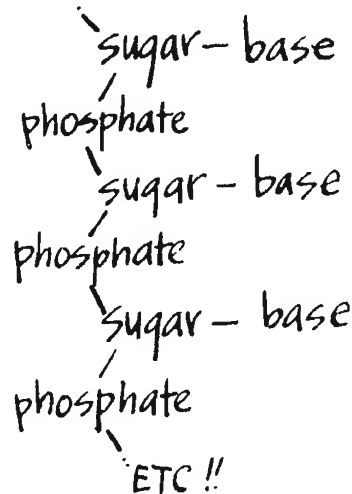
LIPIDS ARE A CLASS OF MORE COMPLEX MACROMOLECULES, HAVING AT LEAST ONE END WHICH IS REPELLED BY WATER. LIPIDS FORM A MAJOR COMPONENT OF CELL MEMBRANES AND INCLUDE THE ANIMAL FATS AND VEGETABLE OILS.

STILL MORE COMPLEX, BUT MOST IMPORTANT IN GENETICS, ARE THE **NUCLEIC ACIDS** AND **PROTEINS**... WATCH CLOSELY:

THE BUILDING BLOCKS FOR NUCLEIC ACIDS ARE CALLED **NUCLEOTIDES**. AN INDIVIDUAL NUCLEOTIDE ITSELF HAS 3 COMPONENTS: A **SUGAR**, A **PHOSPHATE**, AND A **BASE**, LIKE SO —

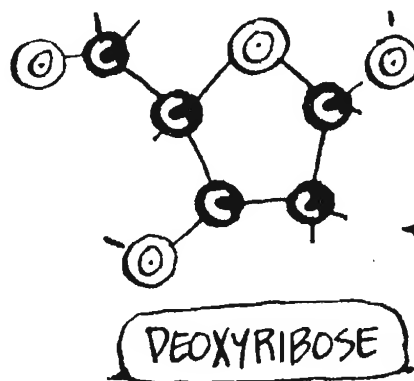
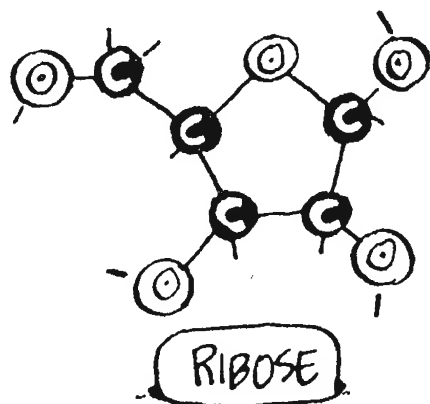


THESE ARE HOOKED TOGETHER TO MAKE A LONGGGGGGG SUGAR-PHOSPHATE "BACKBONE" WITH A SEQUENCE OF BASES STICKING OFF:



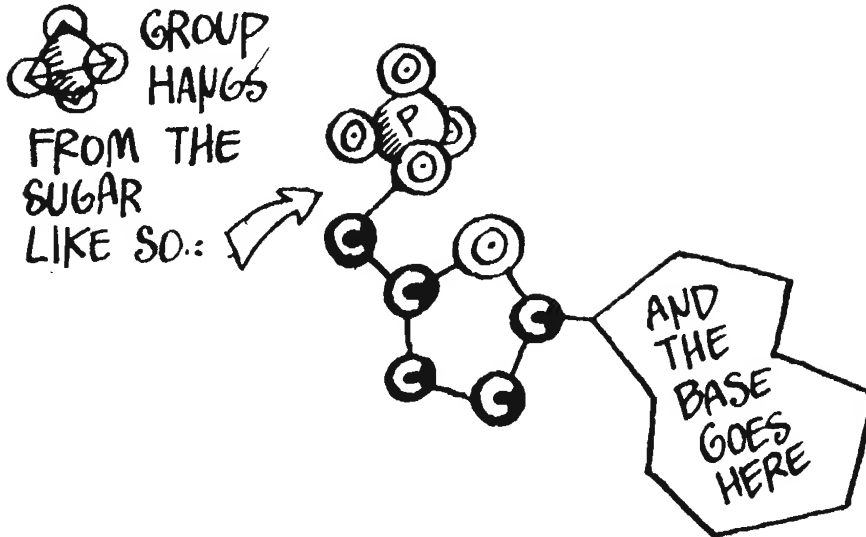
THIS MAY GO ON FOR MILLIONS OF NUCLEOTIDES!

THE SUGAR MAY BE ONE OF TWO KINDS, WHICH WE ILLUSTRATE HERE WITHOUT ALL THEIR PESKY HYDROGEN ATOMS. (THEY JUST CLUTTER UP THE PICTURE!)



← YOU SEE? ONE LESS OXYGEN!

THE PHOSPHATE
GROUP
HANGS
FROM THE
SUGAR
LIKE SO.:

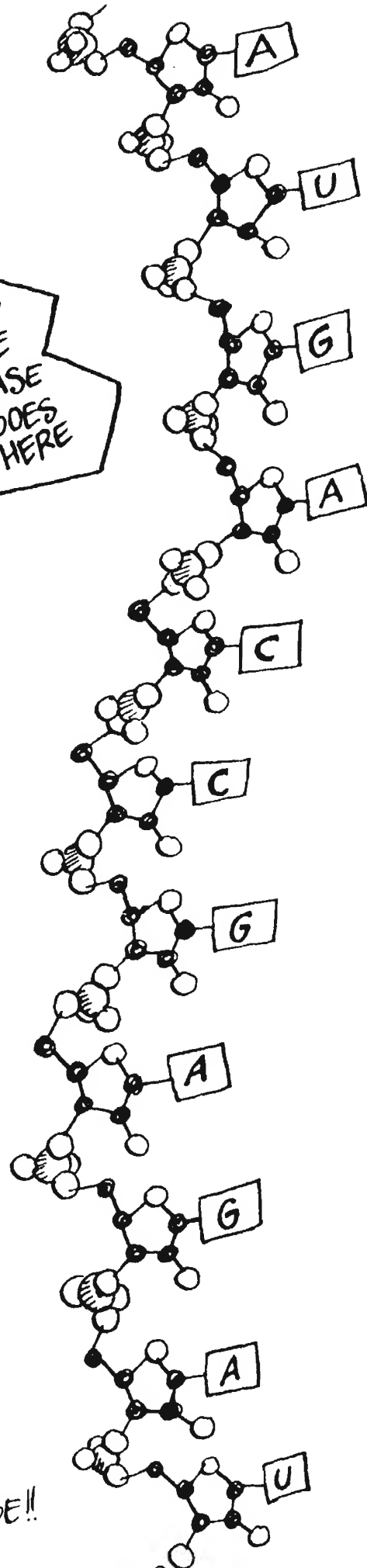


WE'LL TOUCH THE BASES
LATER FOR NOW
WE'LL JUST SAY THERE
ARE 5 KINDS, WITH THE
NICKNAMES A, C, G, T,
AND U.

IN ANY GIVEN NUCLEIC
ACID MACROMOLECULE,
ALL THE SUGARS ARE
THE SAME.

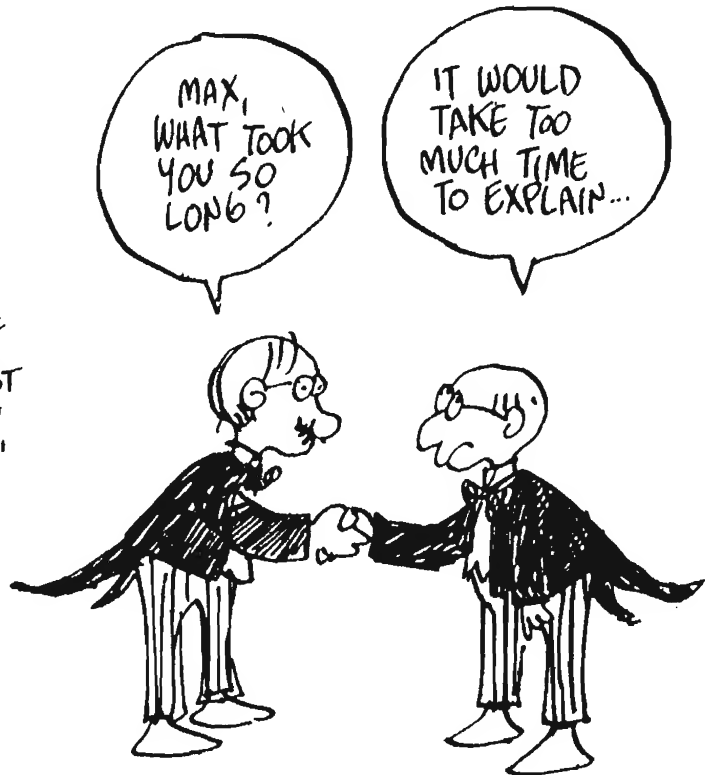
➡ NUCLEIC ACIDS WITH
RIBOSE ARE CALLED
RIBONUCLEIC ACID,
OR RNA. THOSE WITH
DEOXYRIBOSE ARE
CALLED DNA (DEOXY-
RIBONUCLEIC ACID, OF
COURSE!).

IN BOTH DNA AND RNA,
THE BASES MAY BE DIFFERENT
FROM ONE NUCLEOTIDE TO
THE NEXT, GIVING NUCLEIC ACIDS
THE APPEARANCE OF MESSAGES
IN SOME STRANGE MOLECULAR LANGUAGE!!



PROTEINS

ARE THE MOST COMPLICATED MACROMOLECULES OF ALL. THE BIOLOGIST MAX PERUTZ SPENT 25 YEARS — MOST OF HIS CAREER — ANALYZING JUST ONE OF THEM: **HEMOGLOBIN**, THE PROTEIN THAT CARRIES OXYGEN THROUGH THE BLOODSTREAM. FOR THIS, PERUTZ RECEIVED THE NOBEL PRIZE IN 1962...



YET IN A CERTAIN SENSE, PROTEINS ARE SIMPLE, TOO: LIKE OTHER MACROMOLECULES, THEY ARE LONG CHAINS OF SMALLER SUBUNITS.

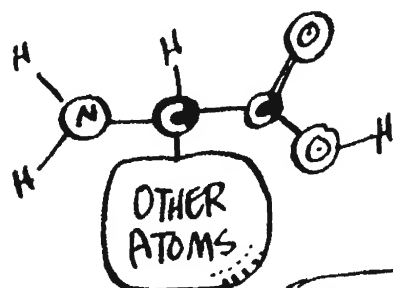


ACTUALLY, HEMOGLOBIN IS TWO PAIR OF SUCH CHAINS, WRAPPED UP IN A SYMMETRICAL TANGLE.

THE SUBUNITS OF PROTEIN MOLECULES ARE **AMINO ACIDS**, WHICH ARE NOT NAMED AFTER **IDI AMIN**, THE FORMER DICTATOR OF UGANDA.



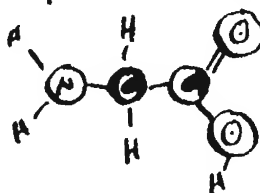
THE TYPICAL AMINO ACID
LOOKS LIKE THIS:



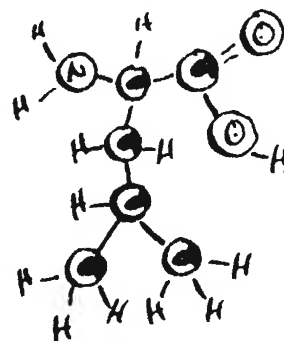
IT'S THAT CLUSTER OF
"OTHER ATOMS" THAT
COMPLICATES MATTERS...



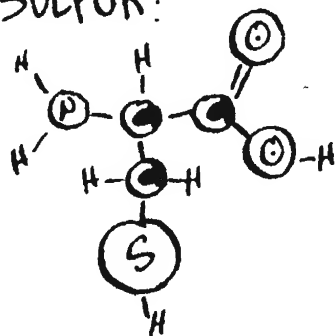
GLYCINE IS
QUITE SIMPLE:



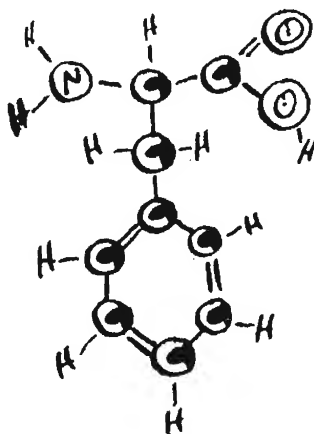
LEUCINE
HAS A BRANCH:



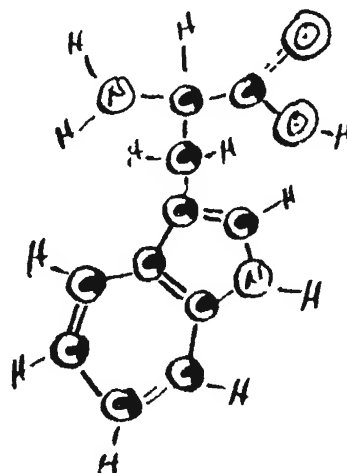
CYSTEINE CONTAINS
SULFUR:



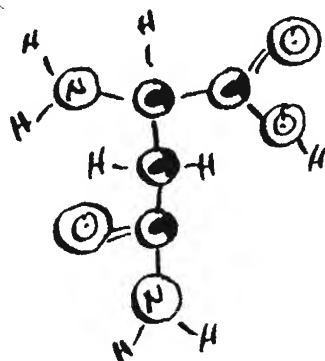
PHENYLALANINE
HAS A RING:



TRYPTOPHAN
HAS RINGS OF
RINGS:



ASPARAGINE HAS
EXTRA NITROGEN:



CONFUSED?
HA HA HA
HA

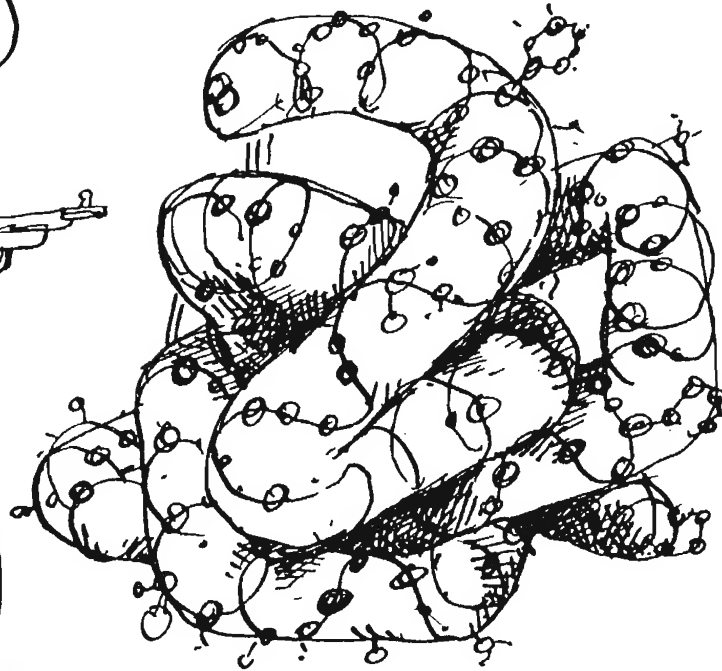


SO WERE
THE CHEMISTS!
HA HA HA HA

NOT ONE
ACID GETS
OUT OF
LINE!!

EVERY PROTEIN HAS A PRECISE NUMBER
AND SEQUENCE OF AMINO ACIDS.
MUTUAL ATTRACTIONS AMONG THEM
CAUSE THE CHAIN TO COIL UP INTO A
FAIRLY COMPACT, BUT FLEXIBLE SHAPE.

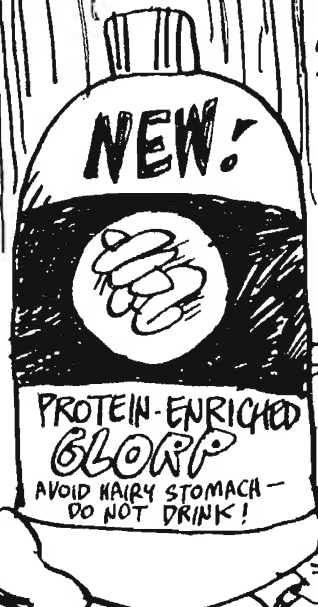
CHUCKLE
CHORTLE



(OFTEN, AS WITH
HEMOGLOBIN, SEVERAL
POLYPEPTIDE CHAINS
MAY COIL TOGETHER.)

WHAT DO PROTEINS
DO FOR A CELL?
YOU PROBABLY THINK
OF THEM AS SOMETHING
THAT ENRICHES
SHAMPOO...
OR MAYBE YOU
KNOW ABOUT THE
PROTEIN IN
FINGERNAILS, FEATHERS,
AND HAIR...
BUT ACTUALLY,
MOST PROTEINS
ARE SOMETHING
ELSE AGAIN...

MOST
PROTEINS
ARE
ENZYMES!!



HA HA
HA
OUCH



ENZYMES ARE PROTEINS WHICH TAKE APART OR PUT TOGETHER OTHER MOLECULES. EACH ENZYME IS RESPONSIBLE FOR JUST ONE SPECIFIC REACTION.

A TYPICAL ENZYME LIES IN WAIT FOR THE RIGHT MOLECULES TO COME AROUND.



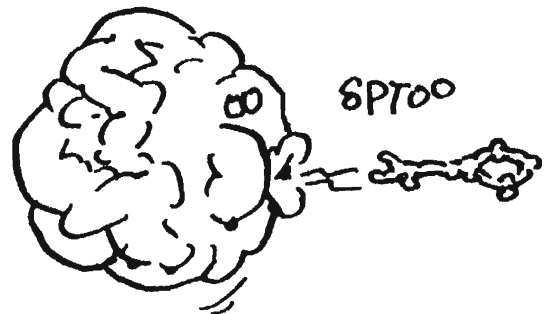
THE ENZYME BINDS TO THE SMALL MOLECULES...



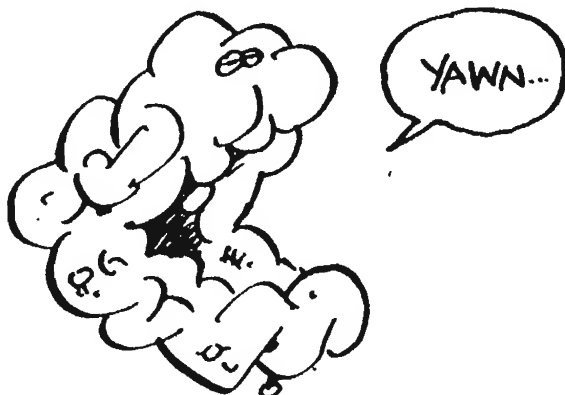
...AND COMBINES THEM...



...INTO A NEW MOLECULE, WHICH IS RELEASED.



THE ENZYME ITSELF REMAINS UNCHANGED IN THE PROCESS.

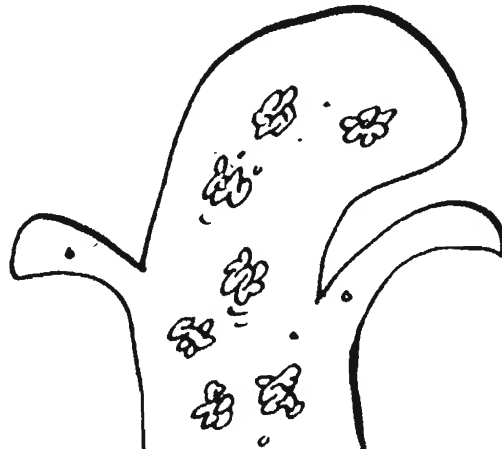


IN A SIMILAR WAY, **DIGESTIVE** ENZYMES BREAK DOWN LARGE MOLECULES. SEVERAL KINDS, FOR EXAMPLE, CHOP SUGARS OFF POLYSACCHARIDES !!



THESE PROTEINS ARE SO IMPORTANT BECAUSE VIRTUALLY EVERY ONE OF LIFE'S CHEMICAL REACTIONS IS DRIVEN BY SOME ENZYME.

WHEN CHEMICALS COME UP THROUGH THE ROOTS OF THE BANANA TREE, THE PLANT'S ENZYMES CONVERT THEM INTO THE CONSTITUENTS OF A BANANA...



MMMM



THEN, WHEN THE GORILLA EATS THE BANANA, THE APE'S ENZYMES DIGEST THE FRUIT AND TURN IT INTO AN APE...

...AND LIKEWISE FOR E. COLI, WHICH HAS ITS OWN ENZYMES...!

IN OTHER WORDS:

An organism
is made by
its enzymes.

AND WHAT
DO YOU SUP-
POSE MAKES
THE ENZYMES?

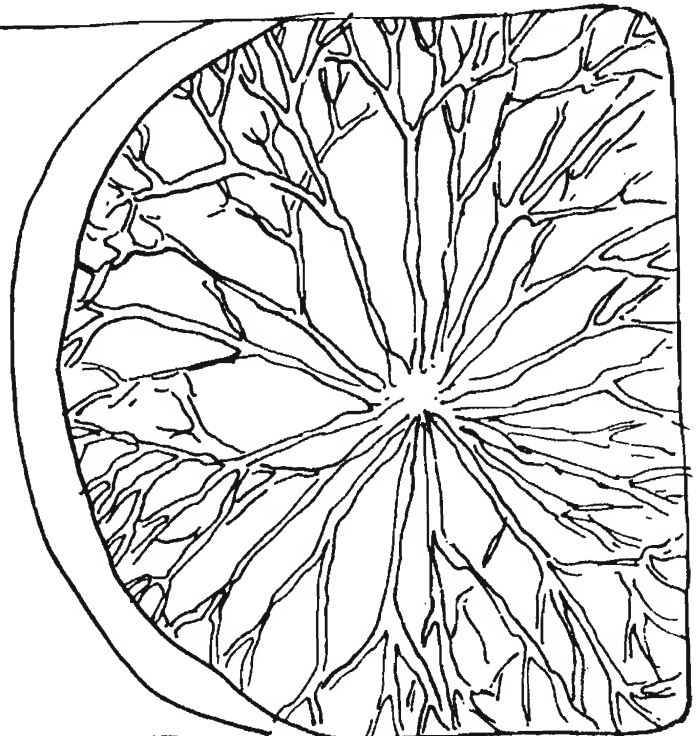


ONE GENE, ONE ENZYME



THE RELATIONSHIP BETWEEN GENES AND ENZYMES FIRST BECAME CLEAR IN THE 1940'S, THANKS TO EXPERIMENTS PERFORMED BY BIOLOGISTS **GEORGE BEADLE** AND **EDWARD TATUM**, WORKING WITH MUTANT STRAINS OF THE COMMON BREAD MOLD **NEUROSPORA** GROWN IN BATHS OF CHEMICAL NUTRIENTS.

EACH MUTANT WAS FOUND TO REQUIRE **MORE CHEMICAL NUTRIENTS** IN ITS DIET THAN WERE NEEDED BY NORMAL MOLD. FOR EXAMPLE, ONE MUTANT HAD TO BE FED AN EXTRA AMINO ACID, WHILE ANOTHER REQUIRED A CERTAIN VITAMIN.



THE REASON, THEY FOUND, WAS THAT NORMAL MOLD WAS ABLE TO MANUFACTURE THE MISSING NUTRIENTS FROM OTHER CHEMICALS...



... WHILE THE MUTANTS COULD NOT— BECAUSE THEY **LACKED SOME OF THE ENZYMES** NECESSARY TO DO SO...



BY EXHAUSTIVE CROSS-BREEDING AND BIOCHEMICAL ANALYSIS, THE SCIENTISTS DISCOVERED THIS: **THE MUTATION OF A SINGLE GENE LED TO THE LACK OF A SINGLE ENZYME...**



* * * * *

The metabolic role of the genes is to make enzymes, and each gene is responsible for one, specific enzyme.



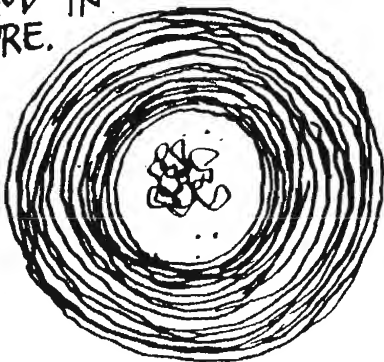
IN SHORT:
**ONE GENE,
ONE ENZYME !!**

SO THAT'S WHAT GENES **DO**—MAKE ENZYMES—BUT STILL NOBODY UNDERSTOOD EXACTLY WHAT THEY **WERE**... THOUGH A FIRST STEP IN THAT DIRECTION HAD BEEN MADE IN THE 1920'S BY **FRED GRIFFITH**...

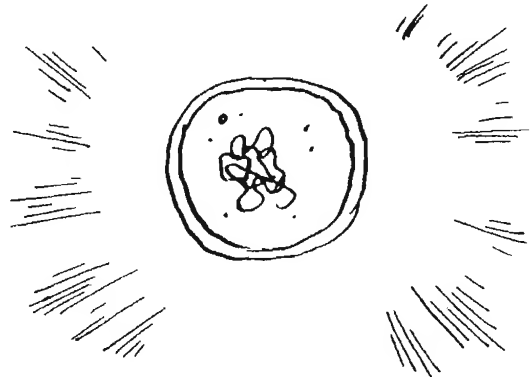
BY ACCIDENT, REALLY!



GRIFFITH WORKED WITH TWO STRAINS OF THE PNEUMONIA BACTERIUM **PNEUMOCOCCUS**. ONE WAS THE VIRULENT "WILD TYPE" FOUND IN NATURE.



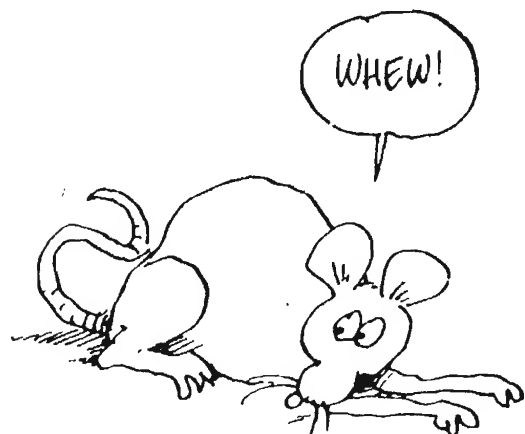
THE OTHER LACKED A CERTAIN ENZYME USED IN MAKING THE THICK OUTER CAPSULE SEEN IN THE WILD TYPE.



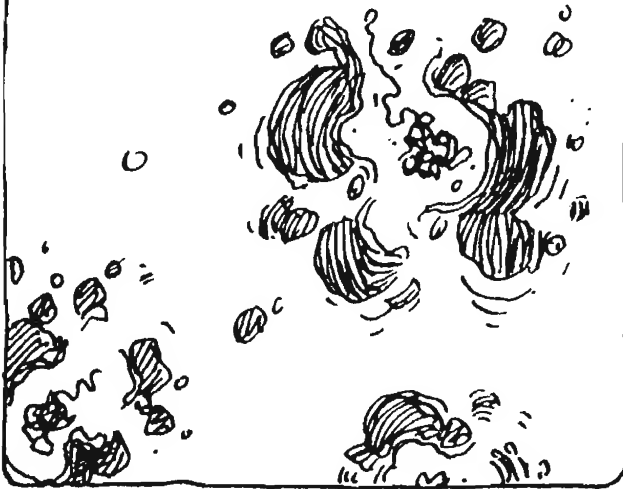
WHEN INJECTED INTO MICE, THE WILD TYPE INVARIABLY CAUSED DISEASE...



THE MUTANT **PNEUMO-COCCUS**, ON THE OTHER HAND, HAD NO EFFECT.



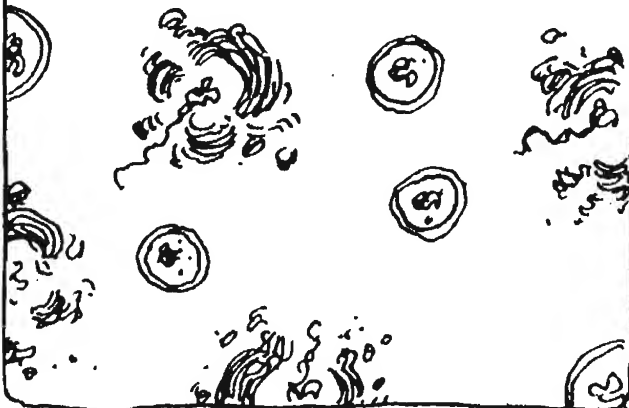
NOW GRIFFITH BOILED SOME OF THE WILD TYPE, MANGLING AND KILLING THEM.



AS EXPECTED, THESE HEAT-KILLED BACTERIA DID NO HARM.



THEN, JUST TO BE THOROUGH, GRIFFITH MIXED SOME **HEAT-KILLED WILD TYPE** WITH **LIVE MUTANTS**.



DESPITE THE FACT THAT EACH INGREDIENT WAS HARMLESS IN ITSELF —



NOT ONLY DID THE MICE DIE, BUT **LIVE WILD-TYPE PNEUMOCOCCUS** WERE FOUND IN THEIR BODIES! GRIFFITH COULDN'T FIGURE THIS OUT AT ALL !!!



EVENTUALLY, IT WAS UNDERSTOOD THIS WAY:



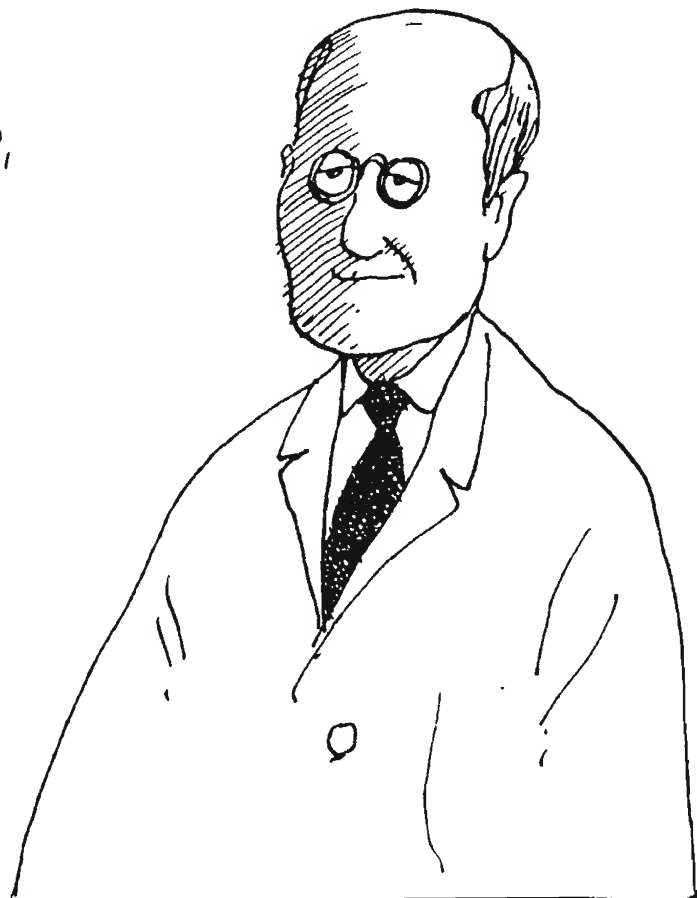
THE **GENES** OF THE WILD TYPE HAD SURVIVED THE BOILING AND INFILTRATED THE LIVE MUTANTS, **TRANSFORMING** THE HARMLESS BACTERIA INTO THE DEADLY WILD TYPE !!



IN THE 1940'S, **OSWALD AVERY** SET OUT TO IDENTIFY THIS "TRANSFORMING FACTOR."

BOILING BACTERIA
BY THE VATFUL,
AVERY PRECIPITATED,
EXTRACTED,
CENTRIFUGED,
ANALYZED,
OVER AND OVER...

UNTIL HE HAD
A THIMBLEFUL
OF PURE
GENETIC
MATERIAL...





WHEN AVERY ANNOUNCED HIS RESULTS IN 1940, FEW SCIENTISTS BELIEVED HIM!!

THE SPIRAL STAIRCASE

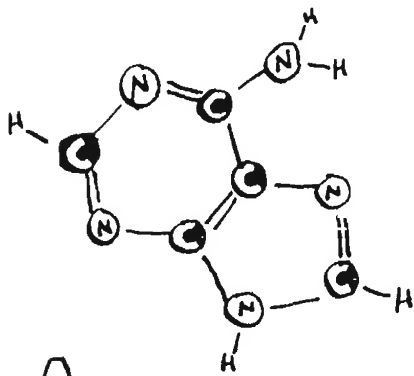
DNA?
IS THAT A
GOVERNMENT
AGENCY?



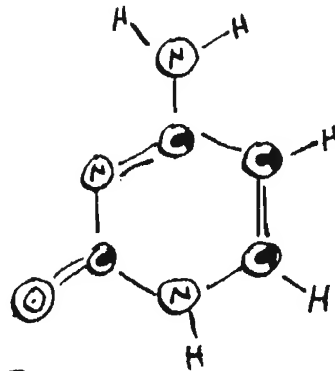
BEFORE AVERY,
SCIENTISTS HAD
PAID LITTLE
ATTENTION TO DNA.

THEY KNEW IT
CONTAINED THE SUGAR
DEOXYRIBOSE,
PLENTY OF **PHOSPHATE**,
AND FOUR **BASES**.

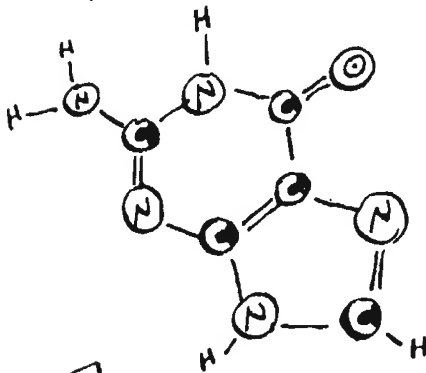
THE FOUR BASES ARE KNOWN AS **A, C, G, AND T**, WHICH
ARE SHORT FOR:



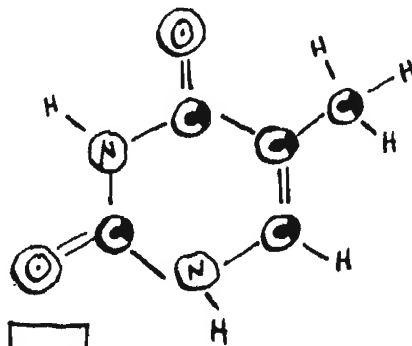
A DENINE



CYTOSINE



GUANINE



THYMINE

THESE WERE ASSUMED TO BE PRESENT IN EQUAL PROPORTIONS.

AFTER AVERY, HOWEVER, RESEARCHERS BEGAN TO LOOK MORE CLOSELY...

ERWIN CHARGAFF FOUND.



① THE COMPOSITION OF DNA VARIED FROM ONE SPECIES TO ANOTHER, IN PARTICULAR IN THE RELATIVE AMOUNTS OF THE BASES A, C, T, G.

② IN ANY DNA, THE NUMBER OF A'S WAS THE SAME AS THE NUMBER OF T'S; SIMILARLY, THE NUMBER OF C'S WAS EQUAL TO THE NUMBER OF G'S.

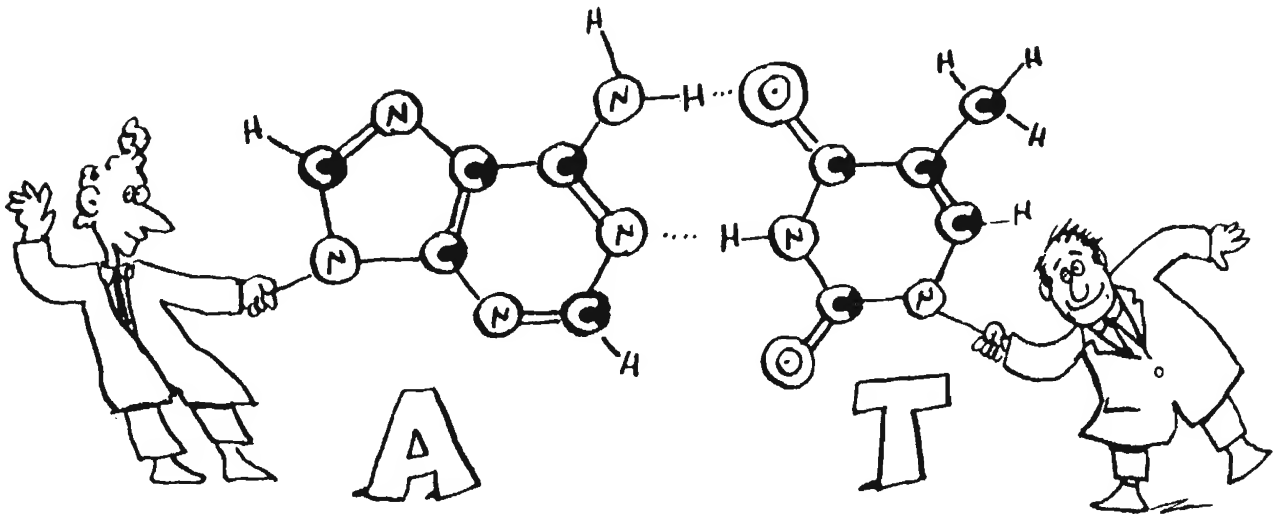
WHAT DID THIS MEAN?
CHARGAFF COULDN'T SAY...

BY STUDYING X-RAY PICTURES OF DNA, ROSALIND FRANKLIN WAS ABLE TO SHOW THAT THE DNA MOLECULE PROBABLY HAD THE CORKSCREW SHAPE OF A **HELIX** WITH TWO OR THREE CHAINS...

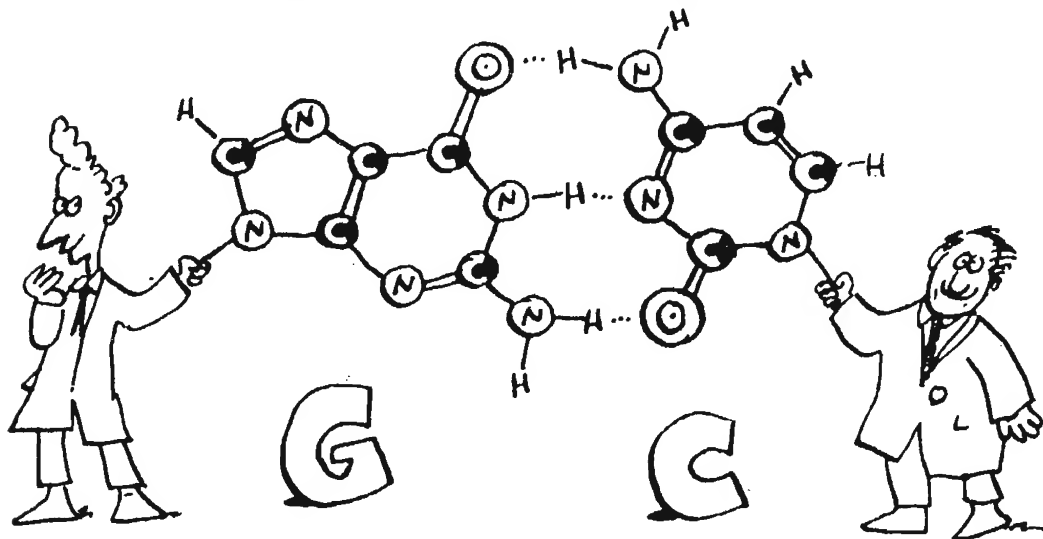
BUT WAS IT TWO OR THREE...?



IN 1952 JAMES WATSON AND FRANCIS CRICK CRACKED THE PUZZLE.



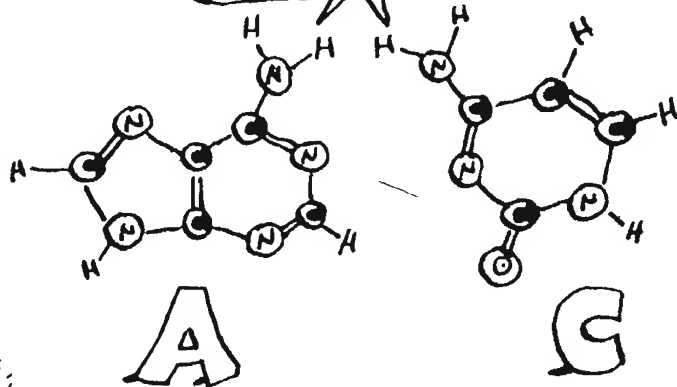
BY PLAYING WITH SCALE-MODEL ATOMS, THEY OBSERVED THAT **ADENINE** FITTED TOGETHER WITH **THYMINE**, WHILE **GUANINE** PAIRED NATURALLY WITH **CYTOSINE**.



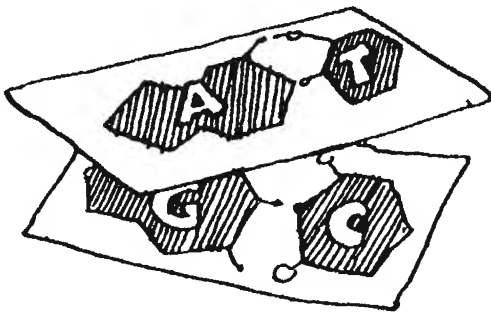
EACH BASE PAIR WOULD BE HELD TOGETHER BY **HYDROGEN BONDING**, A WEAK ATTRACTION THAT MAY OCCUR BETWEEN A HYDROGEN ON ONE MOLECULE AND A NON-HYDROGEN ATOM ON ANOTHER MOLECULE.

IT WAS ALSO CLEAR **A** DID NOT FIT WITH **C**, NOR **G** WITH **T**.

YOU REPEL ME!!



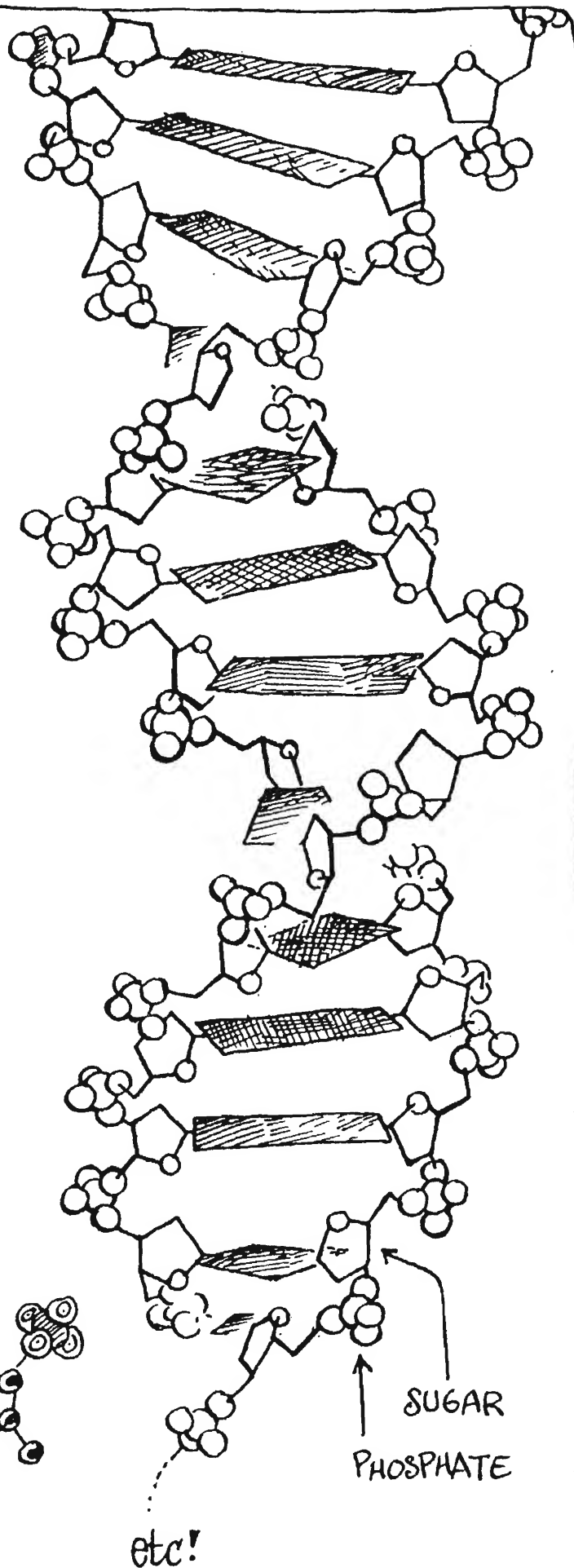
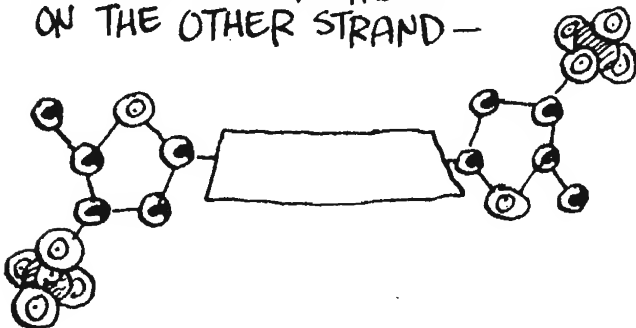
EACH OF THESE TWO
BASE PAIRS IS
NEARLY FLAT:

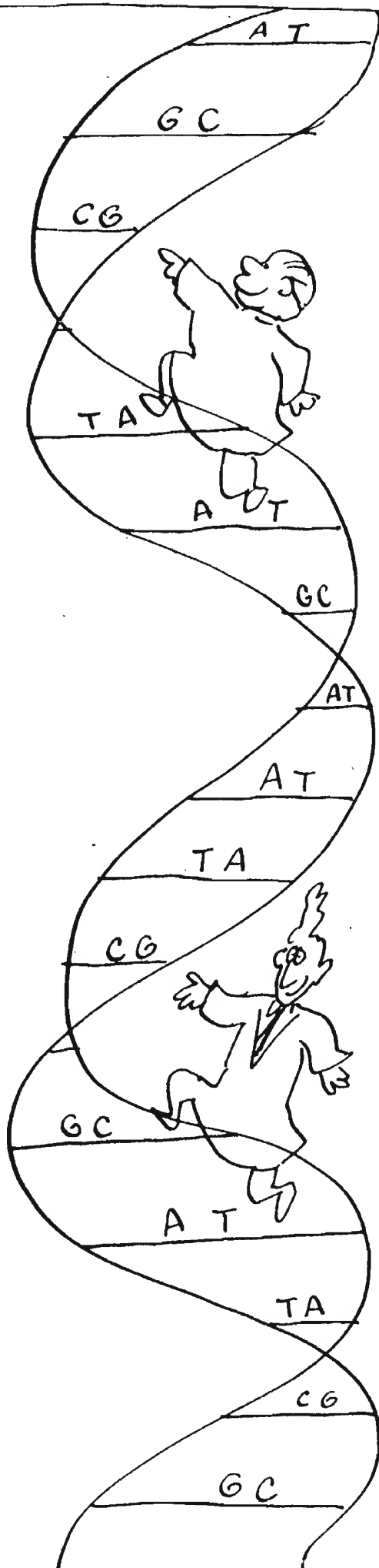


SO WATSON AND
CRICK PROPOSED TO
STACK THEM UP,
ONE AFTER ANOTHER,
LIKE STAIRSTEPS.
TWO SUGAR-PHOSPHATE
STRANDS WIND
AROUND THE
OUTSIDE.



ONE COMPLICATION:
THE TWO STRANDS
WIND IN **OPPOSITE**
DIRECTIONS: THE
SUGARS ON ONE STRAND
ARE "UPSIDE DOWN"
COMPARED WITH THOSE
ON THE OTHER STRAND —





THIS MODEL CLEARLY EXPLAINS CHARGAFF'S OBSERVATION THAT THE NUMBER OF T'S IS EQUAL TO THE NUMBER OF A'S: T AND A ARE ALWAYS PAIRED TOGETHER!

DITTO FOR G AND C!



THIS IS THE PRINCIPLE OF COMPLEMENTARITY: EACH BASE CAN PAIR WITH ONLY ONE OTHER, CALLED ITS COMPLEMENT.

WATSON AND CRICK GOT THE IDEA!! THEY WROTE:

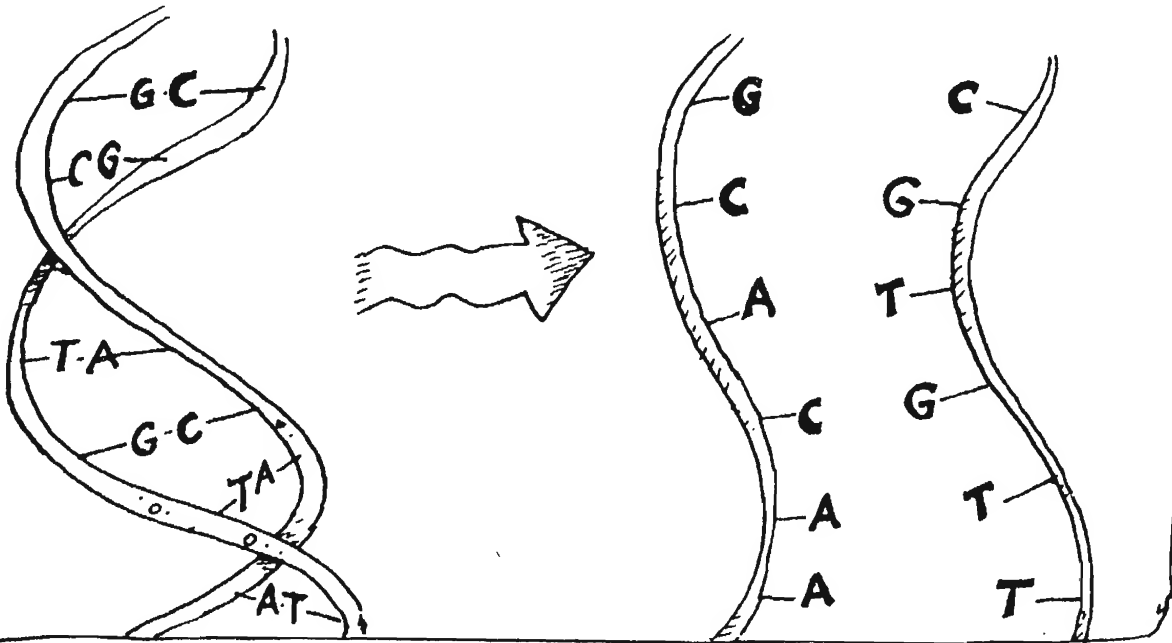
"It has not escaped our notice that the pairing... immediately suggests a possible copying mechanism for the genetic material."

IN FACT, IT IS THE KEY TO THE GENE'S MAIN FUNCTIONS: REPLICATION AND PROTEIN SYNTHESIS.

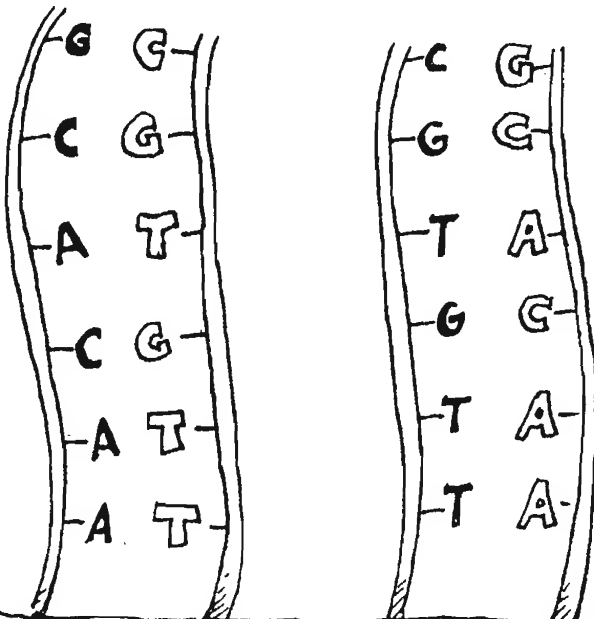
REPLICATION

GENE-COPYING, OR DNA REPLICATION, AS WATSON AND CRICK SAW, IS SIMPLE IN PRINCIPLE. EACH STRAND OF THE DOUBLE HELIX CONTAINS THE INFORMATION NECESSARY TO MAKE ITS COMPLEMENTARY STRAND.

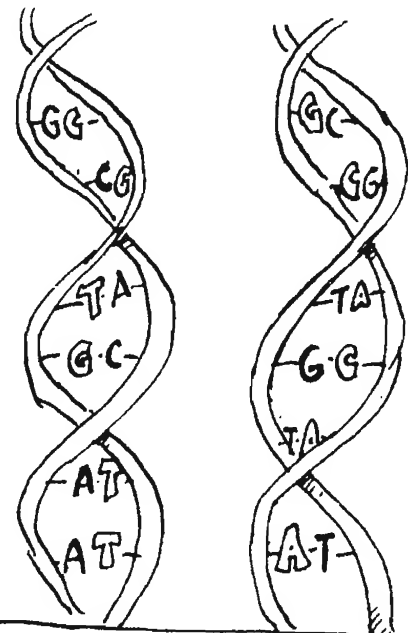
SCHEMATICALLY, IT WORKS LIKE THIS: WHEN THE DNA IS READY TO MULTIPLY, ITS TWO STRANDS PULL APART:



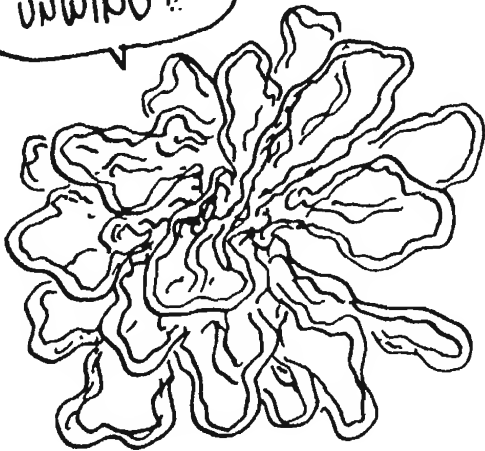
ALONG EACH ONE, A NEW STRAND FORMS IN THE ONLY POSSIBLE WAY:



WE WIND UP WITH TWO COPIES OF THE ORIGINAL!

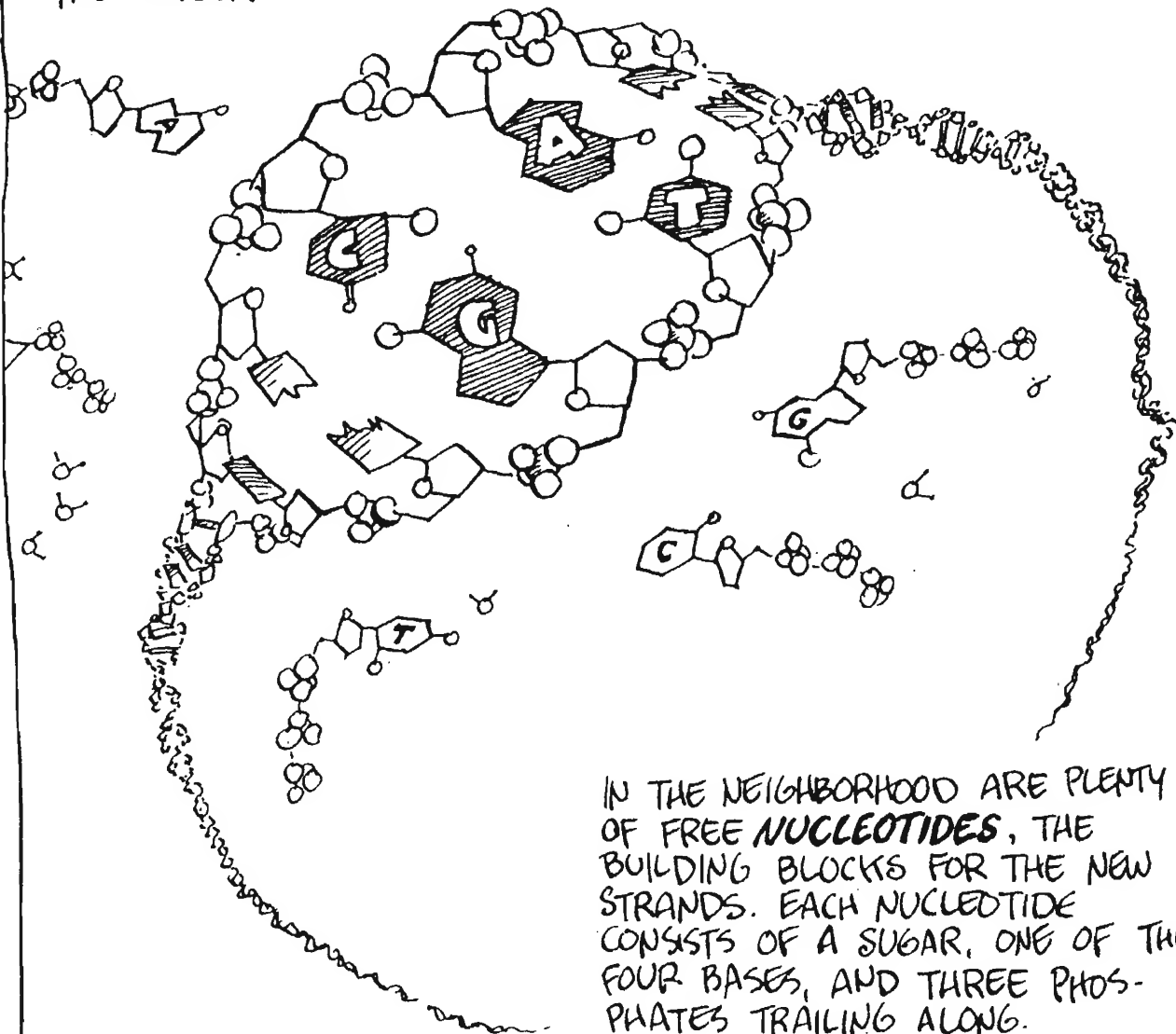


I NEED TO
UNWIND !!



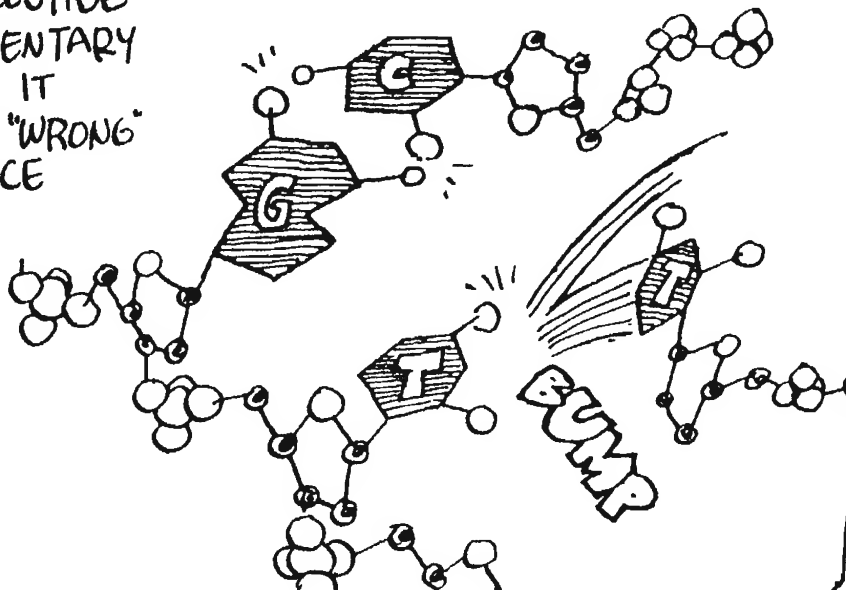
IN PRACTICE, THE
PROCESS OF REPLICA-
TION IS FAR MORE
COMPLICATED.
EVEN IN THE MUCH-
STUDIED *E. COLI*
IT IS IMPERFECTLY
UNDERSTOOD.

IN *E. COLI* REPLICATION BEGINS WHEN A "SNIPPING" ENZYME
CUTS THE DNA STRANDS APART AT A SMALL REGION CALLED
THE **ORIGIN**.

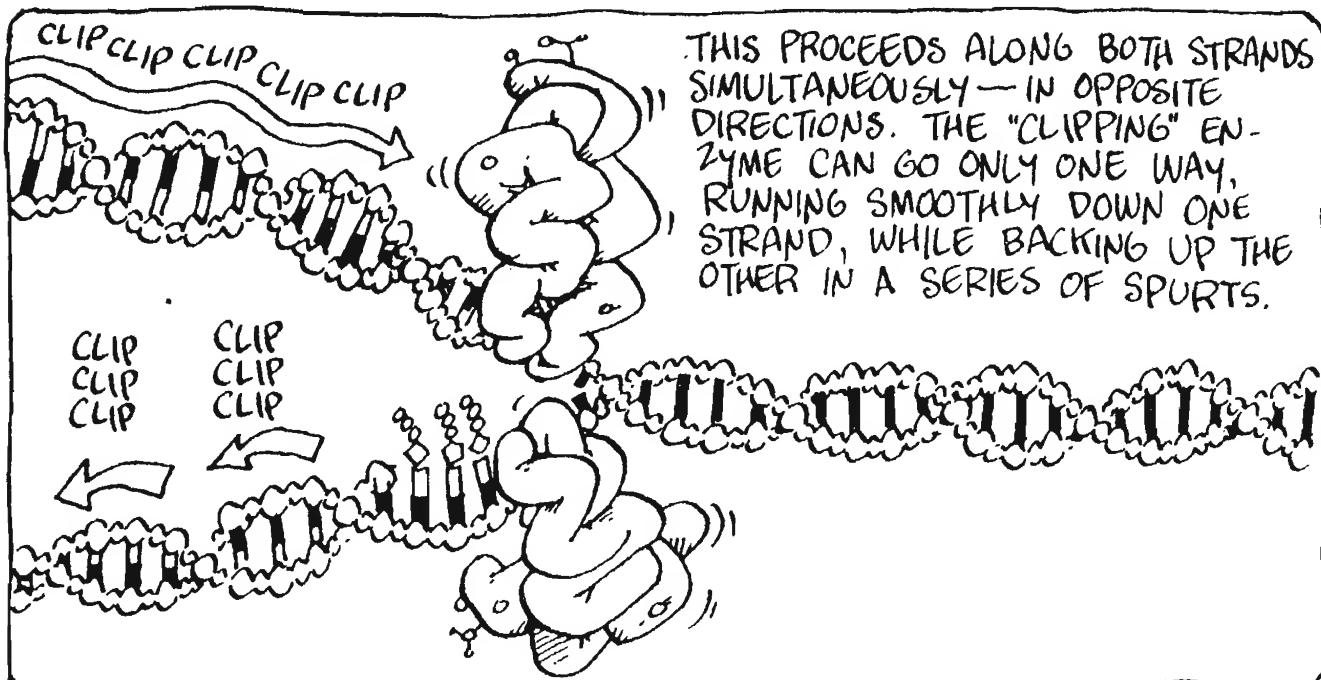
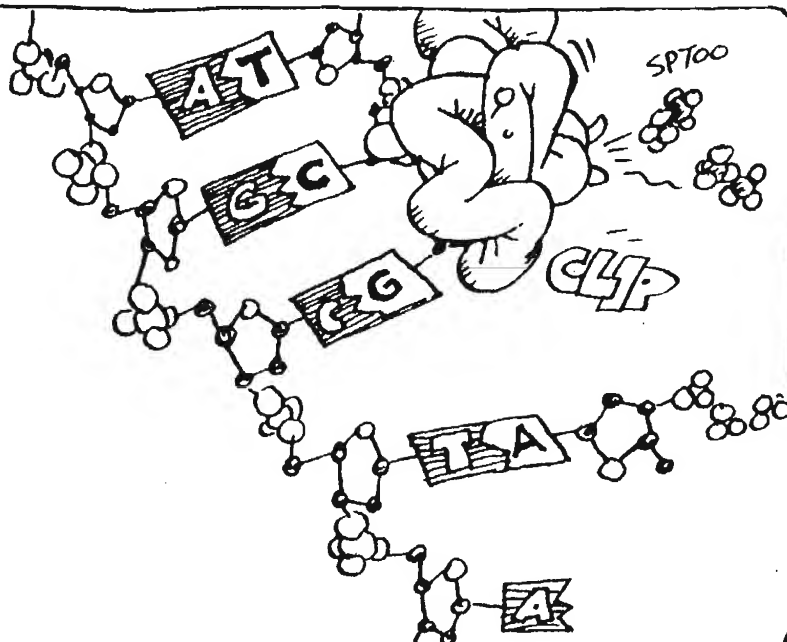


IN THE NEIGHBORHOOD ARE PLENTY
OF FREE **NUCLEOTIDES**, THE
BUILDING BLOCKS FOR THE NEW
STRANDS. EACH NUCLEOTIDE
CONSISTS OF A SUGAR, ONE OF THE
FOUR BASES, AND THREE PHOS-
PHATES TRAILING ALONG.

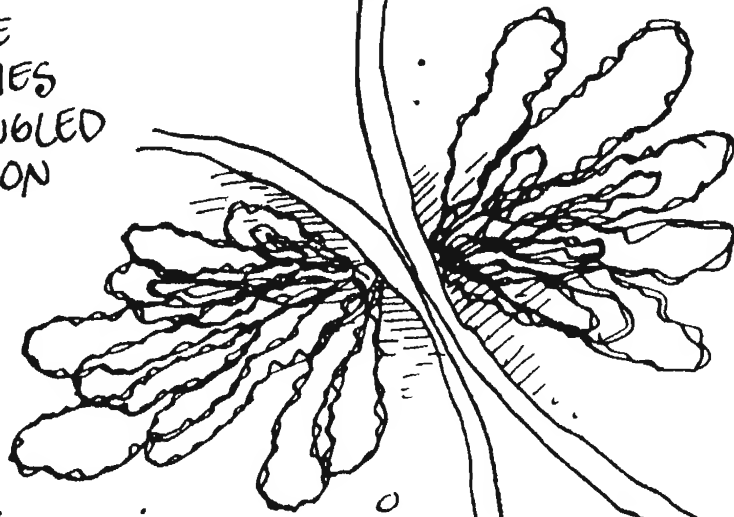
WHEN A FREE NUCLEOTIDE MEETS ITS COMPLEMENTARY BASE ON THE DNA, IT STICKS, WHILE THE "WRONG" NUCLEOTIDES BOUNCE AWAY.



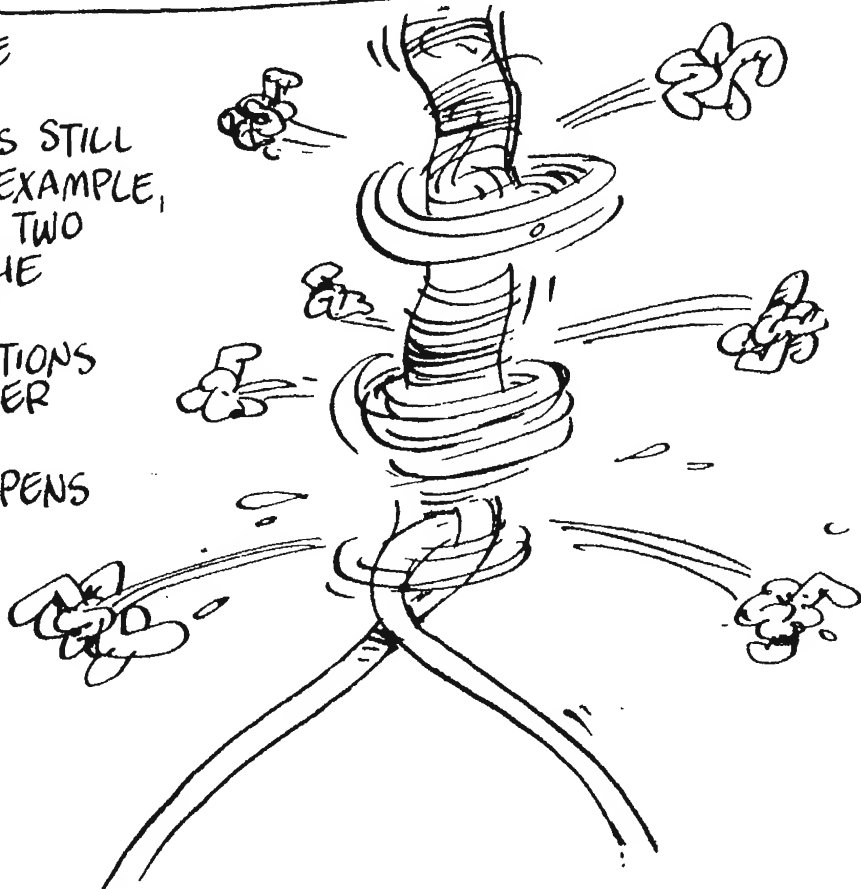
AS THE "SNIPPING" ENZYME OPENS THE DNA FURTHER, MORE NUCLEOTIDES ARE ADDED, AND A "CLIPPING" ENZYME PUTS THEM TOGETHER, KNOCKING OFF THE EXTRA PHOSPHATES.



ONCE REPLICATED, THE TWO NEW CHROMOSOMES HAVE TO BE DISENTANGLED SO THAT CELL DIVISION CAN OCCUR.



THE PICTURE WE HAVE OF DNA REPLICATION IS STILL SKETCHY. FOR EXAMPLE, UNWINDING THE TWO STRANDS OF THE DOUBLE HELIX INVOLVES ROTATIONS AT SPEEDS OVER 8000 RPM. HOW THIS HAPPENS IS STILL NOT WELL UNDERSTOOD.

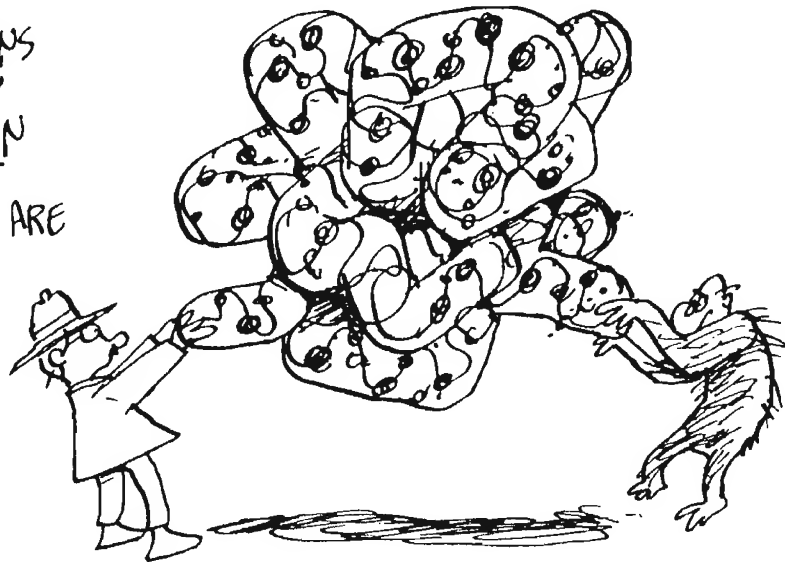


WHATEVER THE DETAILS, THE PRINCIPLE OF COMPLEMENTARITY IS THE KEY TO REPLICATION, AS WELL AS TO THE GENE'S SECOND MAIN FUNCTION:



The MOLECULE is the MESSAGE

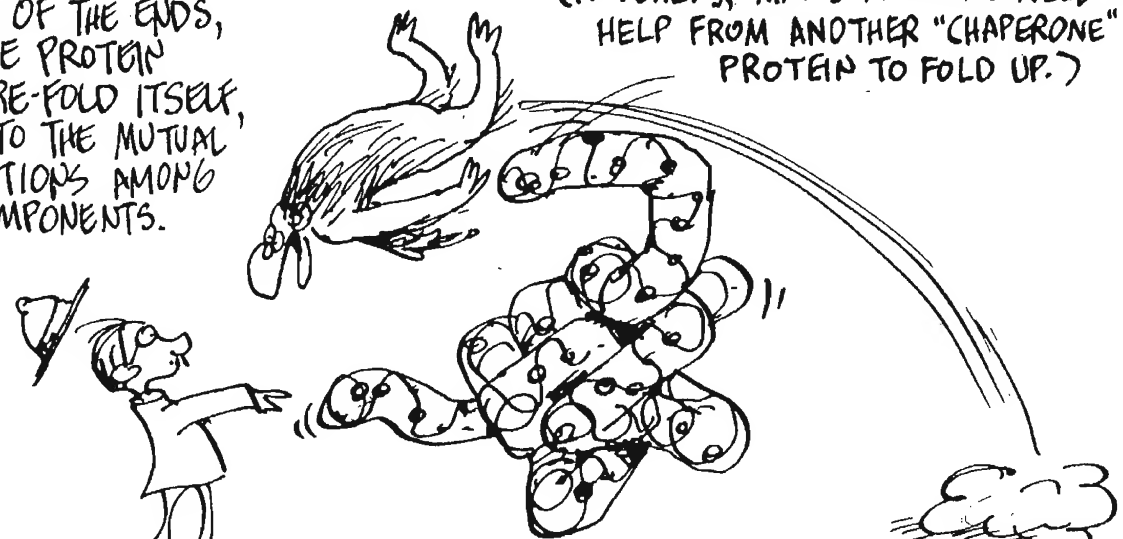
ENZYMES AND OTHER PROTEINS COME IN MANY SHAPES, BUT IN AN IMPORTANT RESPECT, THEY ARE ALL ALIKE.



UNFOLD ANY PROTEIN, AND YOU'LL FIND IT'S SIMPLY A CHAIN OF AMINO ACIDS.

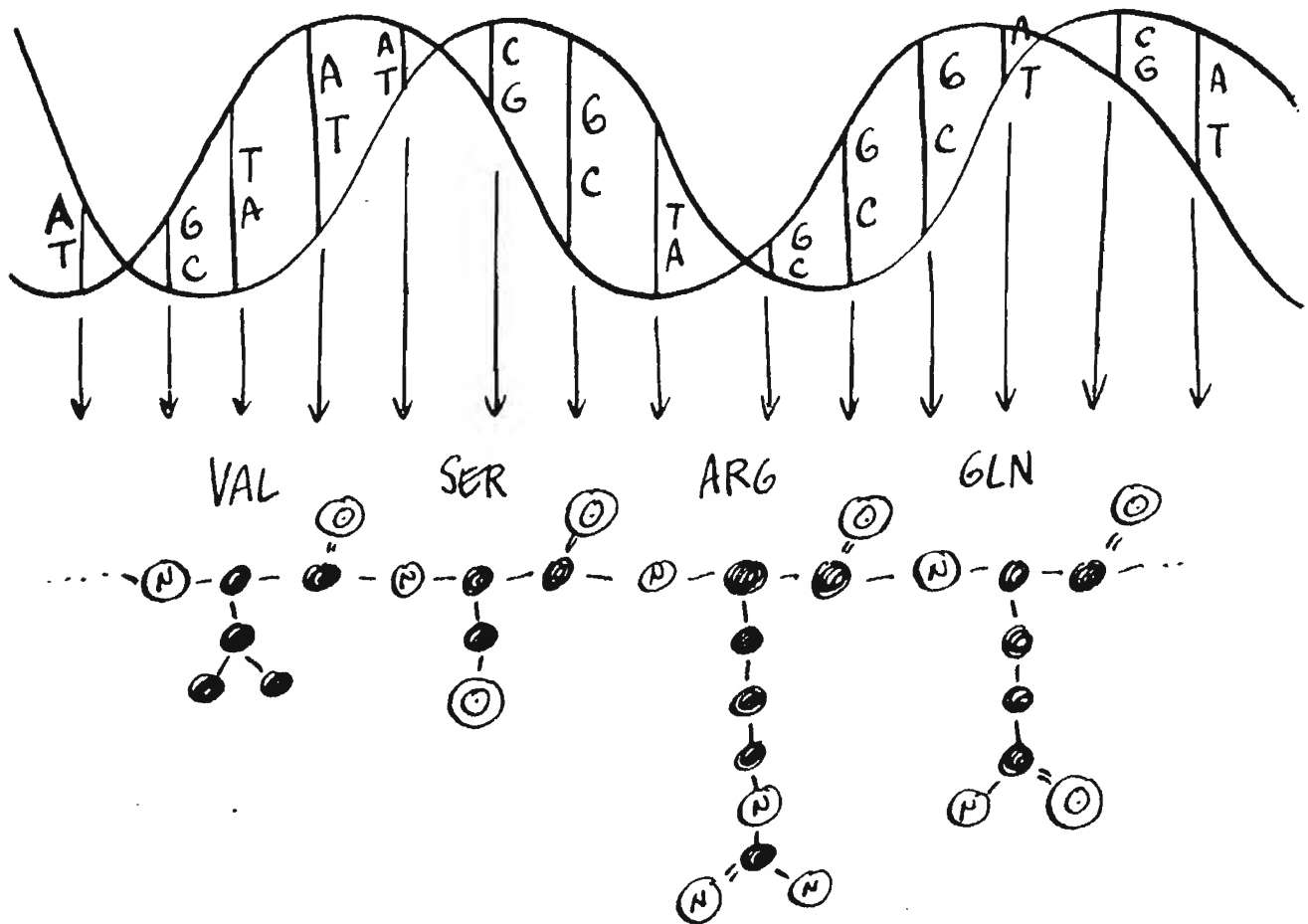
LET GO OF THE ENDS, AND THE PROTEIN WILL RE-FOLD ITSELF, OWING TO THE MUTUAL ATTRACTIONS AMONG THE COMPONENTS.

(ACTUALLY, MANY PROTEINS NEED HELP FROM ANOTHER "CHAPERONE" PROTEIN TO FOLD UP.)

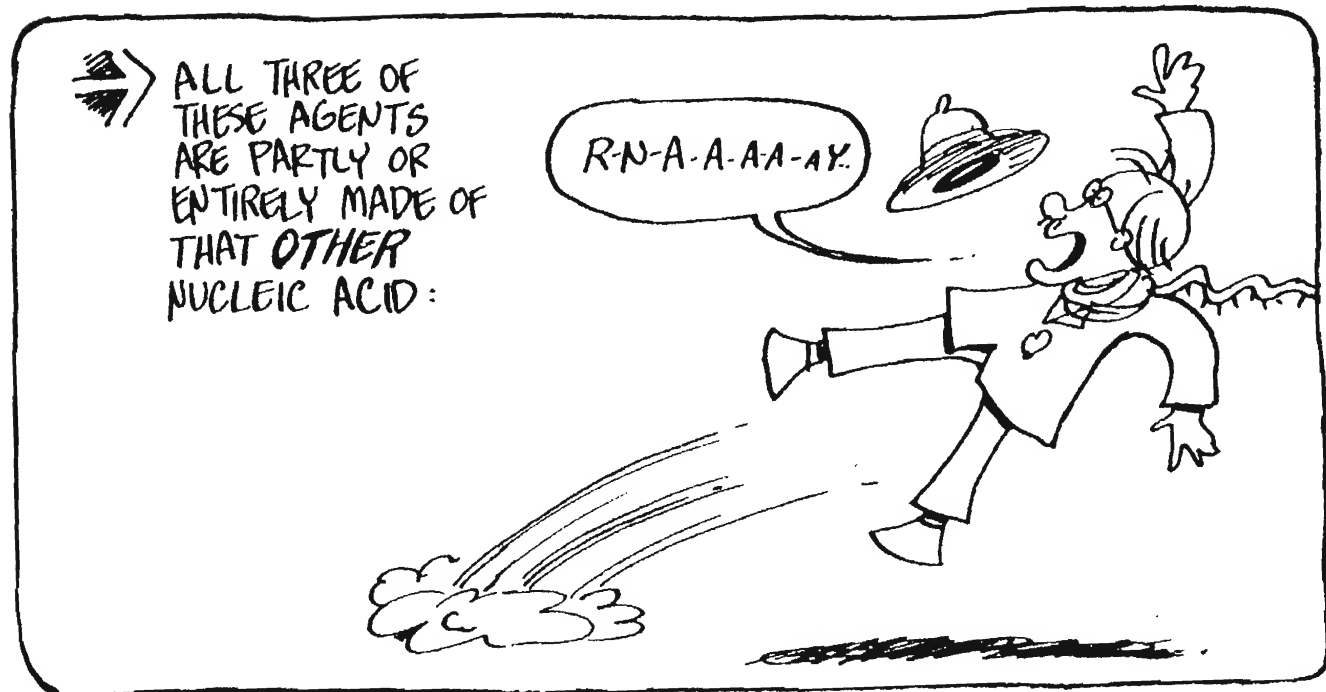
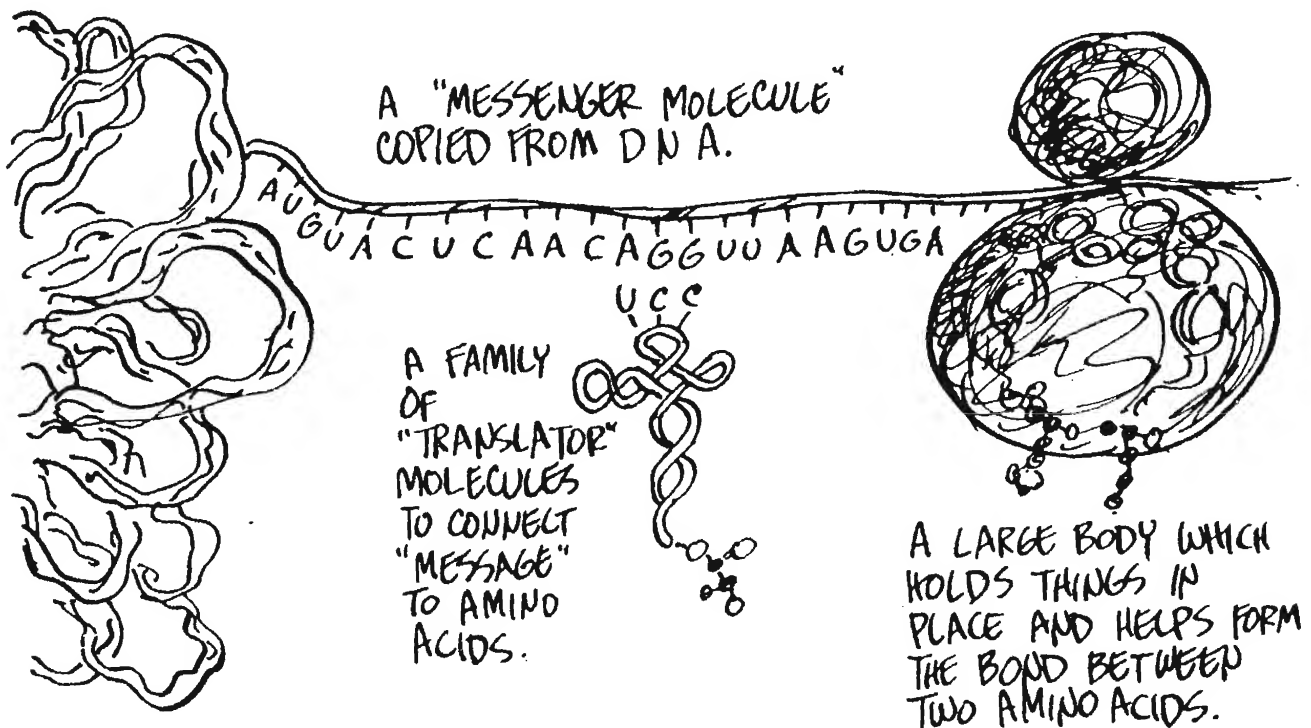
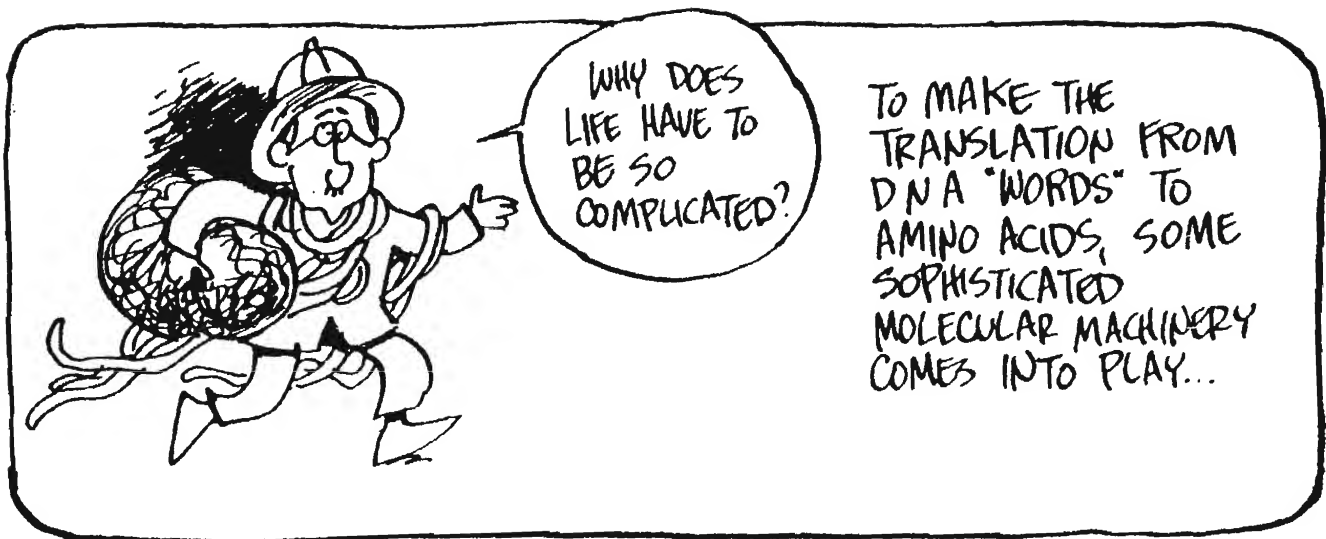


THAT IS: THE SEQUENCE DETERMINES THE STRUCTURE.

IN VIEW OF THE RELATIONSHIP BETWEEN GENES AND PROTEINS,
THIS SUGGESTS THAT THE *SEQUENCE* OF DNA MUST
SOMEHOW PARALLEL OR REFLECT THE *SEQUENCE* OF THE
PROTEIN.



The sequence of
base pairs may be
thought of as a series
of "words" specifying
the order of amino
acids in each protein.



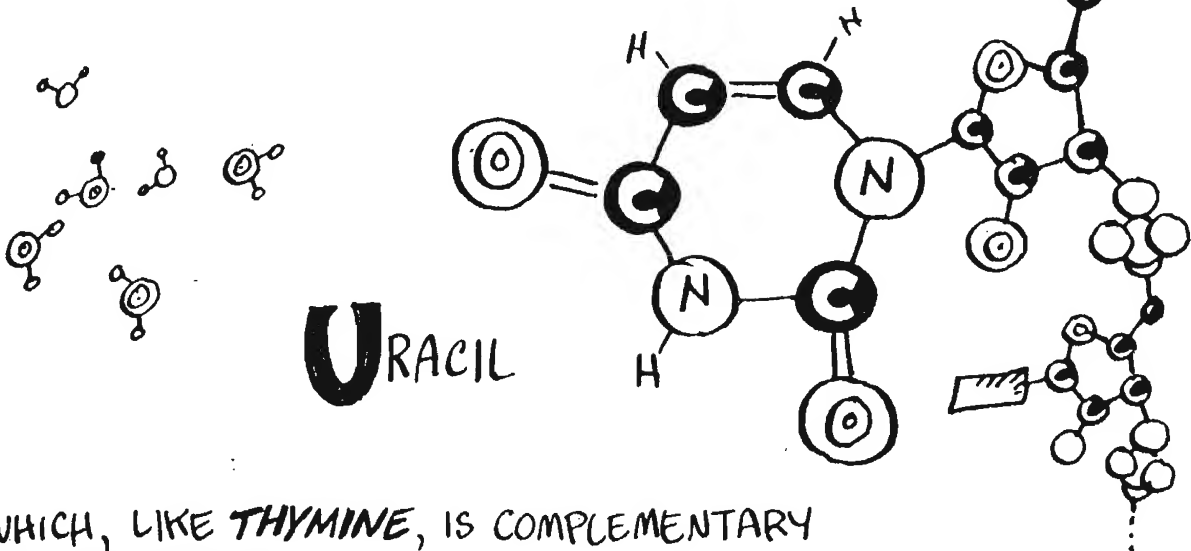
RNA — **RIBONUCLEIC ACID** — RESEMBLES
DNA: A SUGAR-PHOSPHATE BACKBONE
WITH A SERIES OF BASES ATTACHED.



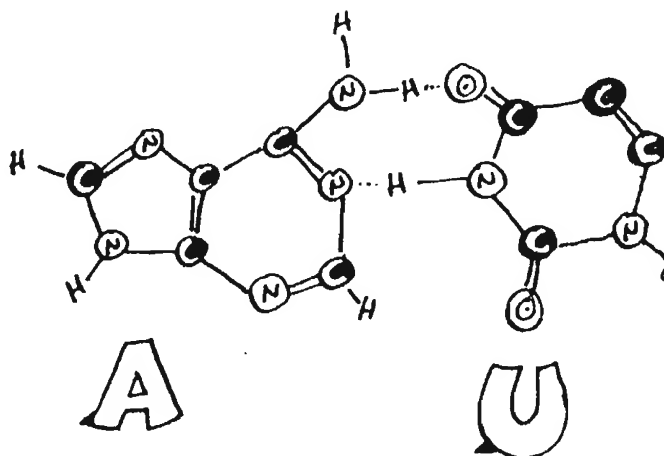
THE
DIFFERENCES:

ITS SUGAR IS **RIBOSE**,
RATHER THAN DEOXYRIBOSE;
RNA IS USUALLY
SINGLE-STRANDED;
AND IT IS MUCH SHORTER —
50 TO 1000 NUCLEOTIDES,
COMPARED WITH A
MILLION OR MORE IN DNA!

AND FINALLY, WHILE THE BASES **A, C, AND G**
ARE THE SAME AS IN DNA, RNA HAS IN
PLACE OF **T** ANOTHER BASE CALLED **URACIL** ("U").



WHICH, LIKE **THYMINE**, IS COMPLEMENTARY
TO **ADENINE**:

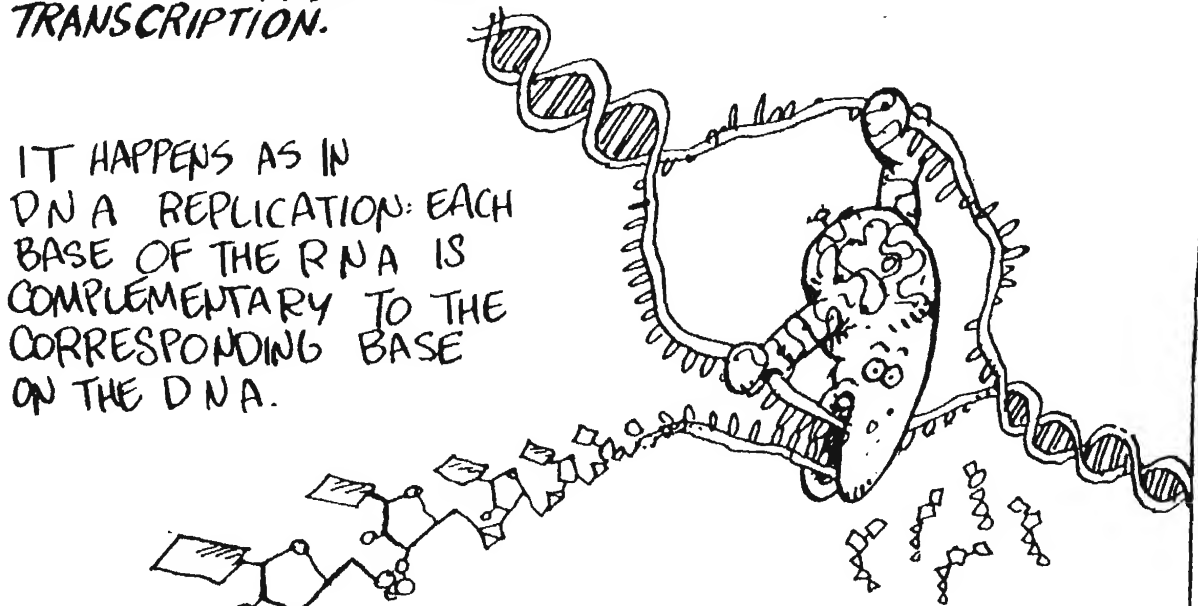


NOW LET'S
SEE HOW
RNA
WORKS !!



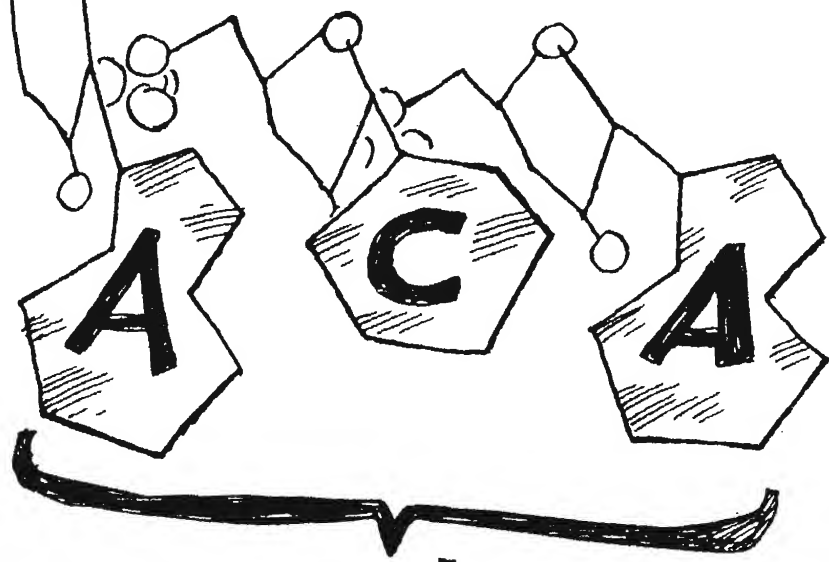
PROTEIN SYNTHESIS BEGINS WHEN A REGION OF DNA IS TEASED APART AND A MOLECULE OF RNA IS BUILT ALONG ONE STRAND BY AN ENZYME CALLED **RNA POLYMERASE**. THIS PROCESS IS CALLED **TRANSCRIPTION**.

IT HAPPENS AS IN DNA REPLICATION: EACH BASE OF THE RNA IS COMPLEMENTARY TO THE CORRESPONDING BASE ON THE DNA.



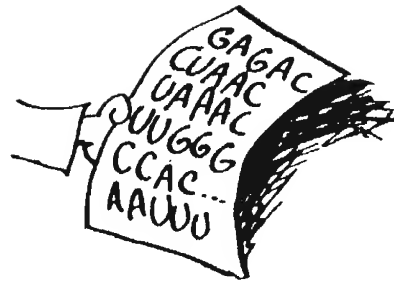
THIS RNA IS CALLED THE **MESSENGER**, OR **mRNA**, BECAUSE IT CARRIES THE GENETIC MESSAGE FROM THE DNA TO THE PROTEIN FACTORY.

THE "WORDS" OF THE MESSAGE ARE **TRIPLETS OF BASES** — A-U-G, A-C-A, ETC. THE TECHNICAL NAME FOR ONE OF THESE GROUPS IS A



codon

EACH 3-BASE CODON STANDS FOR A SINGLE AMINO ACID, AND THE WHOLE mRNA STRAND ENCODES A PROTEIN (OR SEVERAL PROTEINS). IT'S JUST LIKE A MESSAGE IN CODE —



THE GENETIC CODE!



CRACKING THIS CODE BEGAN IN 1961, WHEN MARSHALL NIRENBERG WAS ABLE TO MAKE A SPECIAL mRNA, WHOSE ONLY BASE WAS URACIL, REPEATED OVER AND OVER: "POLY-U."



FROM IT HE OBTAINED A PROTEIN CONSISTING ENTIRELY OF THE AMINO ACID PHENYLALANINE.

SO  UUU WAS THE CODON FOR PHENYLALANINE...

NEXT THEY DECODED POLY-A, AND POLY-C, AND POLY-UG, POLY-UGU, ETC, ETC, ETC, UNTIL THE CODE WAS FINALLY BROKEN —

UUU	→	Phe
AAA	→	Lys
CCC	→	
UGU	→	
GUU	→	
UUG	→	Leu
GUG	→	Val

THE COMPLETE CODE TABLE FOLLOWS!



SECOND LETTER

FIRST LETTER

	U	C	A	G	
U	UUU } PHE UUC } UUA } LEU UUG }	UCU } UCC } SER UCA } UCG }	UAU } TYR UAC } UAA } STOP UAG }	UGU } CYS UGC } UGA } STOP UGG } TRP	U C A G
C	CUU } CUC } LEU CUA } CUG }	CCU } CCC } PRO CCA } CCG }	CAU } HIS CAC } CAA } GLN CAG }	CGU } CGC } ARG CGA } CGG }	U C A G
A	AUU } AUC } ILE AUA } AUG } MET	ACU } ACC } THR ACA } ACG }	AAU } ASN AAC } AAA } LYS AAG }	AGU } SER AGC } AGA } ARG AGG }	U C A G
G	GUU } GUC } VAL GUA } GUG }	GCU } GCC } ALA GCA } GCG }	GAU } ASP GAC } GAA } GLU GAG }	GGU } GGC } GLY GGA } GGG }	U C A G

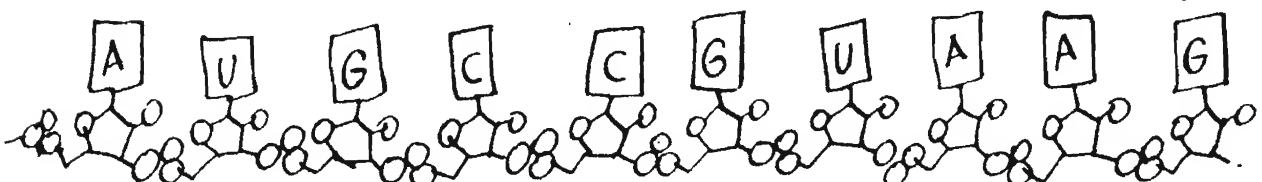
THIRD LETTER



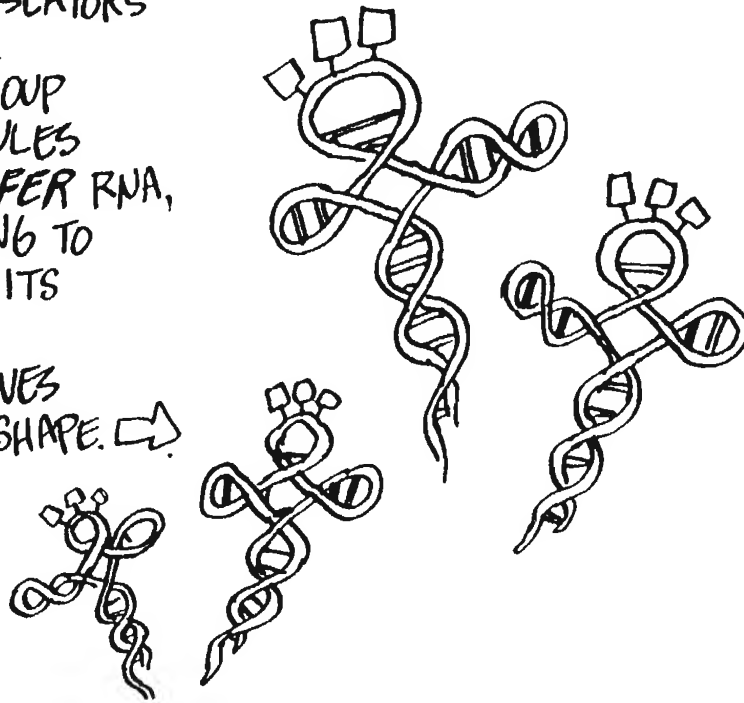
THE CODE IS REDUNDANT: WITH 64 POSSIBLE CODONS, BUT ONLY 20 AMINO ACIDS, THERE MUST BE "SYNONYMS," DIFFERENT CODONS WHICH ENCODE THE SAME AMINO ACID.

THERE ARE "STOP" SIGNALS. THREE CODONS DO NOT ENCODE ANY AMINO ACID AT ALL. THESE SERVE TO TERMINATE MESSAGES.

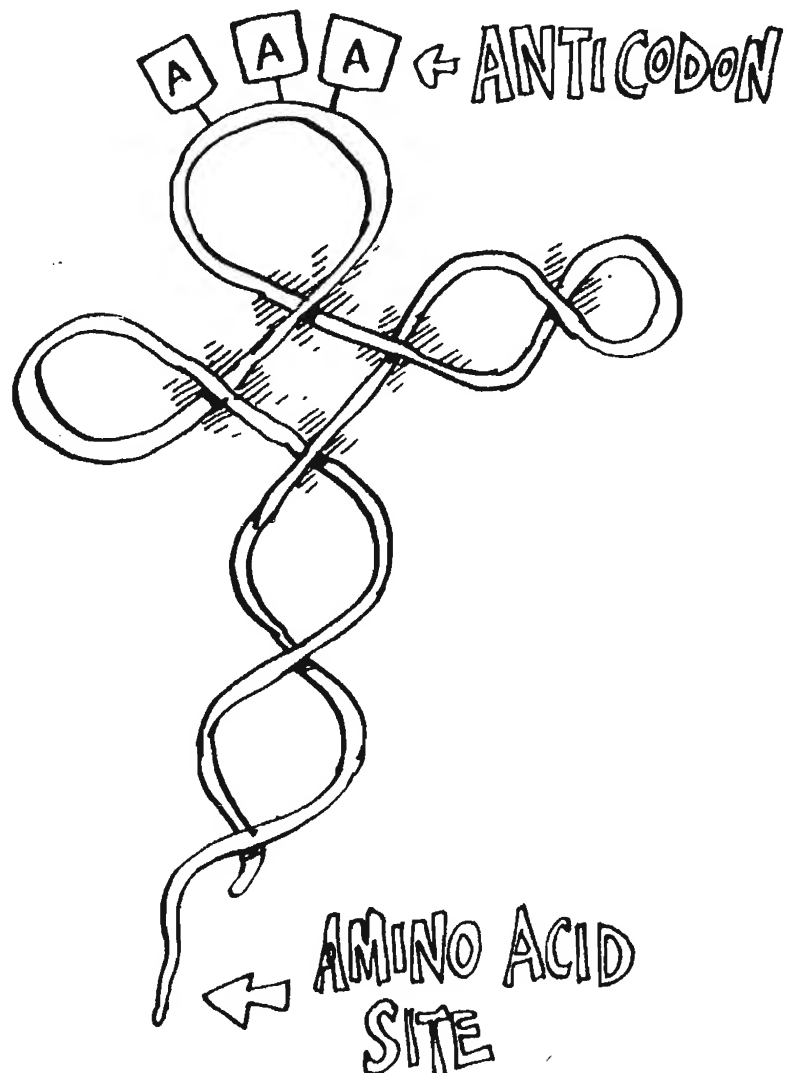
ALSO: THE CODE IS NON-OVERLAPPING. THE "WORDS" FOLLOW EACH OTHER WITHOUT GAPS OR OVERLAPS. WE'LL SEE SHORTLY HOW IT KNOWS WHERE TO START...



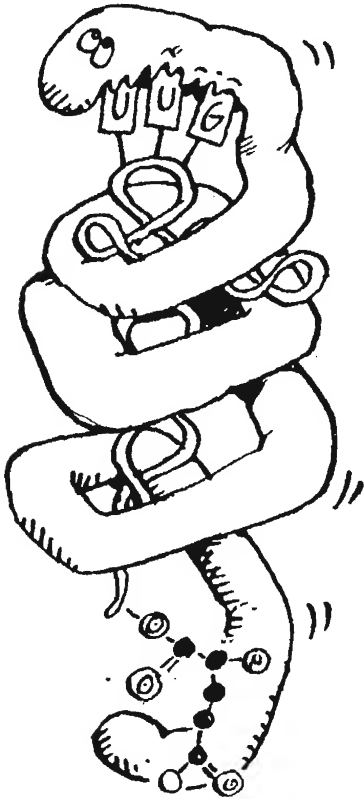
THE ACTUAL TRANSLATORS OF THE GENETIC CODE ARE A GROUP OF RNA MOLECULES CALLED **TRANSFER RNA**, OR **tRNA**. OWING TO PAIRING AMONG ITS BASES, tRNA'S TWIST THEMSELVES INTO THIS KEY SHAPE. →



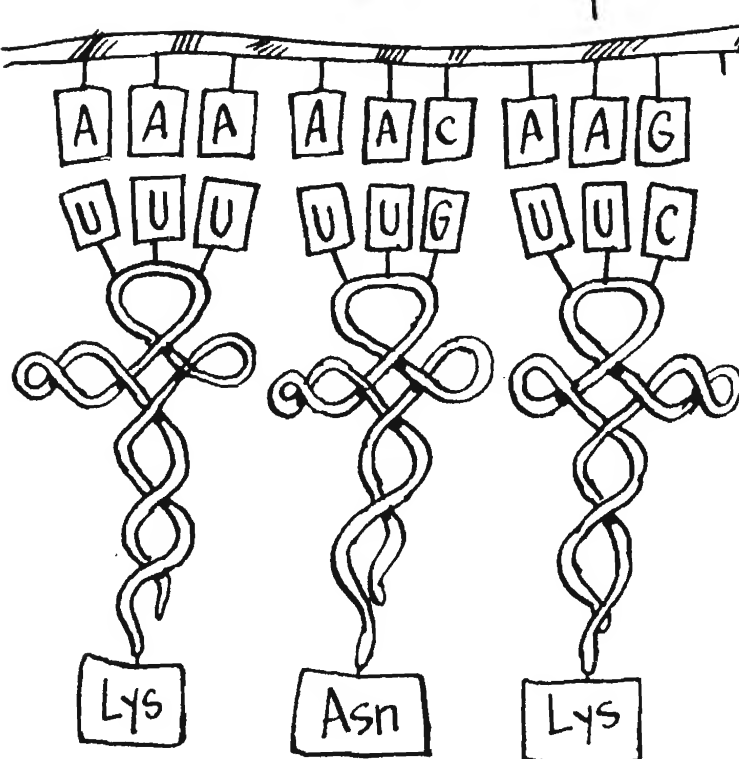
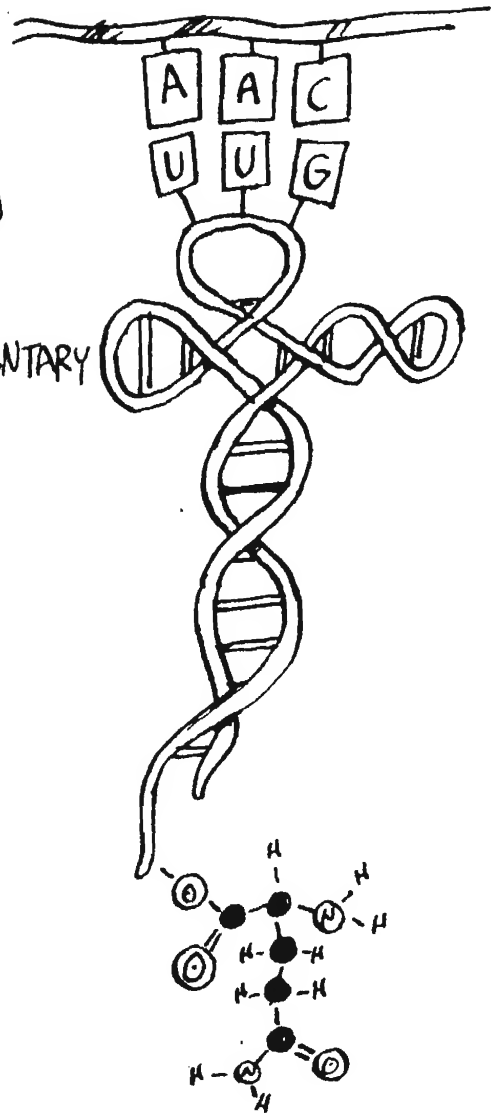
THE LOOP END OF tRNA HAS THREE UNPAIRED BASES. THIS "**ANTICODON**" MAY BIND WITH THE COMPLEMENTARY CODON OF mRNA. AT THE "TAIL" END OF tRNA IS A SITE FOR ATTACHING A SINGLE AMINO ACID.



FOR EACH ANTICODON, THERE IS AN ENZYME WHICH RECOGNIZES IT AND ATTACHES THE APPROPRIATE AMINO ACID TO ITS tRNA.



ONCE THEY ARE LINKED, THE ANTICODON BINDS TO THE COMPLEMENTARY CODON OF MESSAGE.



SCHEMATICALLY, THIS IS THE WAY A STRING OF BASES IS TRANSLATED INTO A SEQUENCE OF AMINO ACIDS.

HOWEVER, THE CELL NEEDS ONE MORE PIECE OF EQUIPMENT TO MAKE IT WORK: THE RIBOSOME.

HOW PROTEINS ARE MADE

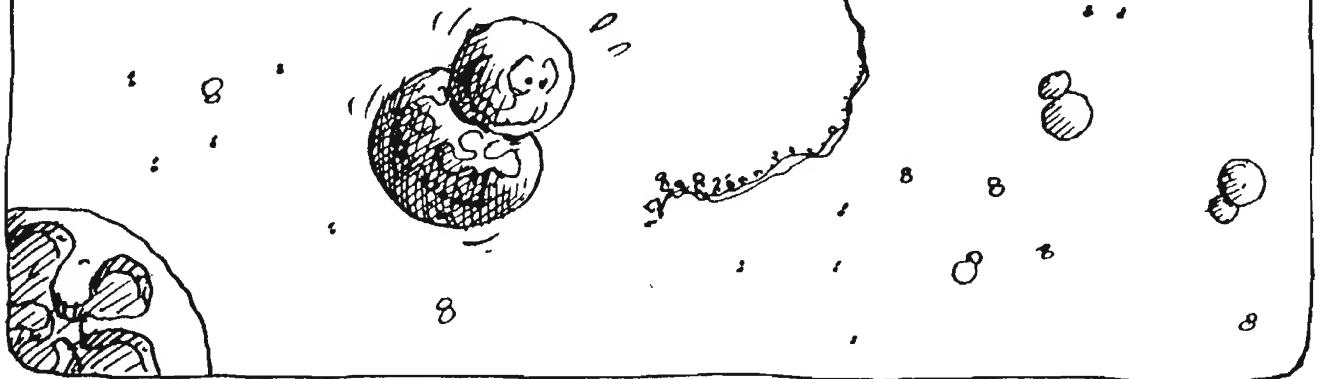
THE FINAL INGREDIENT IN THE PROTEIN-MAKING APPARATUS IS AN OBJECT THAT HOLDS EVERYTHING IN PLACE.

THIS IS THE **RIBOSOME**, A DOUBLE BALL OF ABOUT 50 PROTEINS WRAPPED UP WITH RNA. THIS RNA IS CALLED **RIBOSOMAL RNA**, rRNA FOR SHORT.

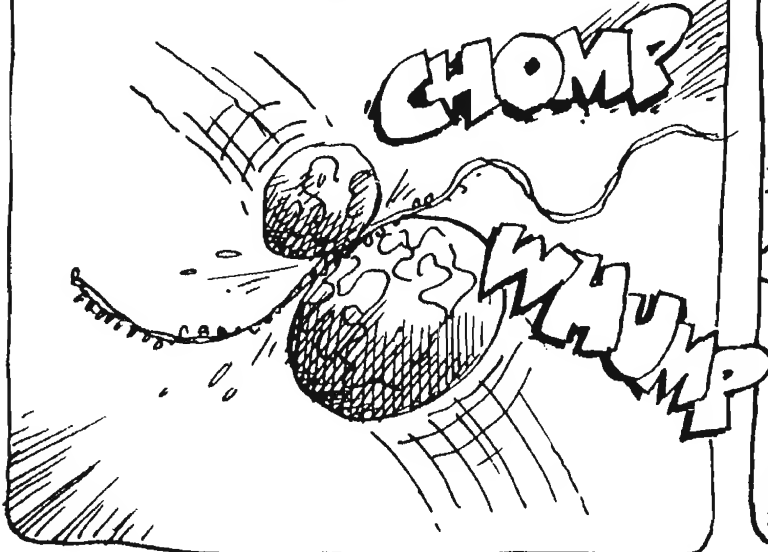


THE RIBOSOME HAS TWO SLOTS IN WHICH MOLECULES OF tRNA CAN FIT SNUGLY.

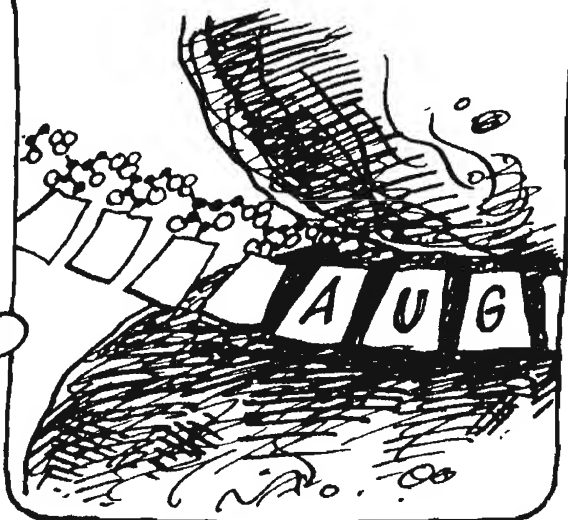
NOW TO MAKE A PROTEIN:
WHEN THE mRNA READS
OUT THE DNA SEQUENCE,
IT ENTERS A SEA
OF RIBOSOMES.



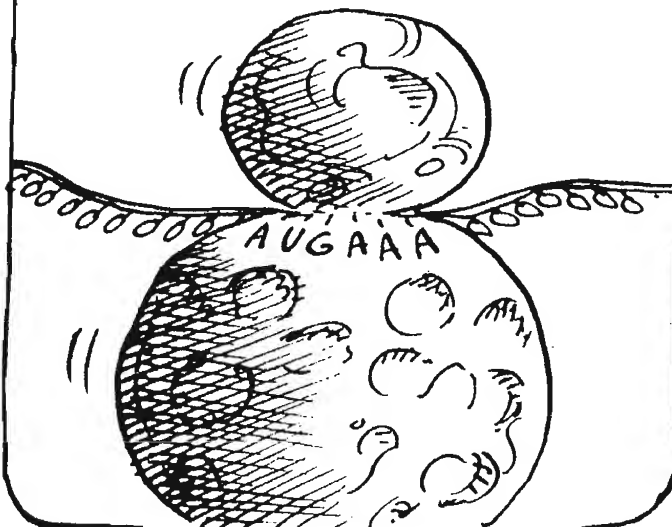
ONE HALF AT A TIME, A RIBO-
SOME BINDS ONTO THE mRNA.



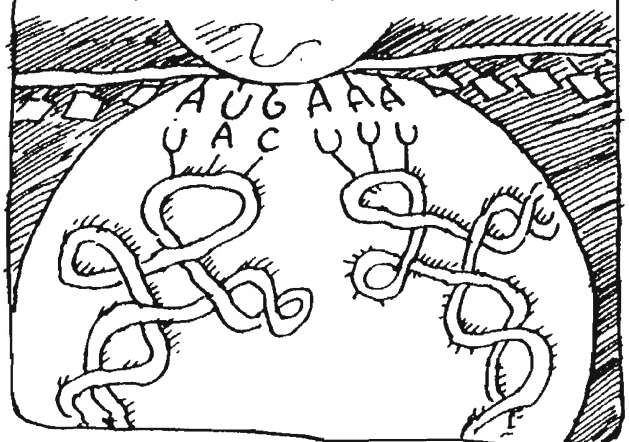
THE BINDING SITE IS
LOCATED AT OR NEAR THE
CODON A·U·G.



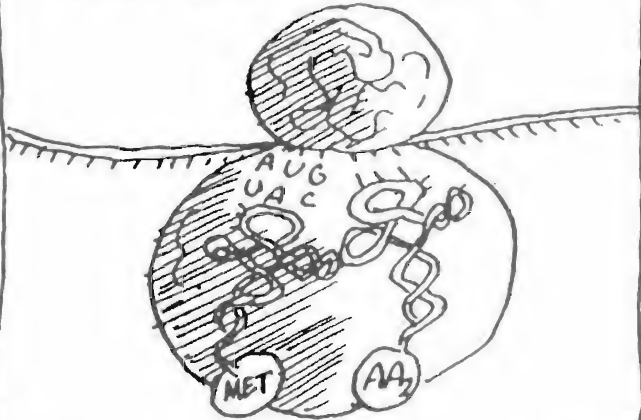
THUS, A·U·G IS ALWAYS THE
FIRST "WORD" OF EVERY MESSAGE.



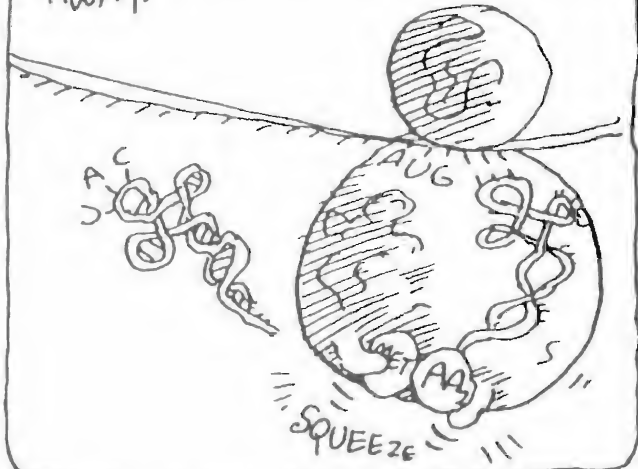
A·U·G AND THE NEXT
CODON EACH BOND WITH
COMPLEMENTARY tRNA'S,
WHICH FIT INTO THE SLOTS
ON THE RIBOSOME.



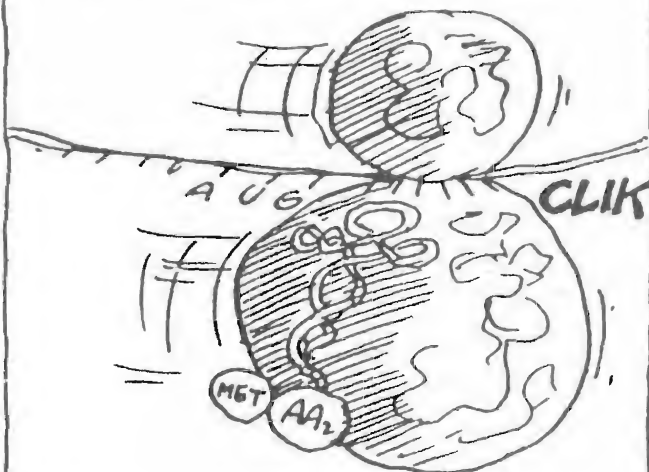
EACH tRNA CARRIES AN AMINO ACID (AA), THE FIRST ONE ALWAYS BEING METHIONINE, WHICH GOES WITH A·U·G.



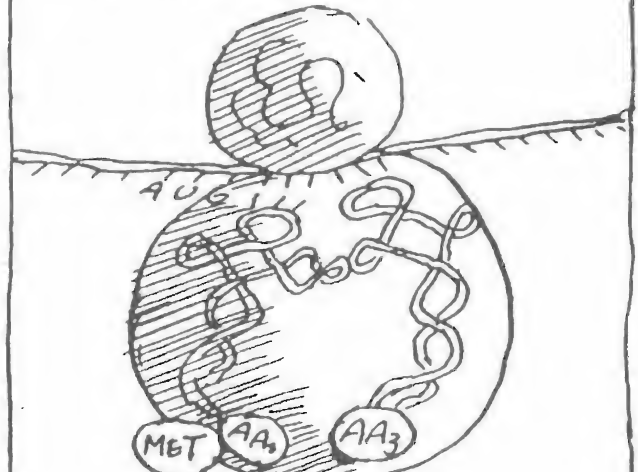
AN ENZYME IN THE RIBOSOME LINKS THE TWO AMINO ACIDS, AND THE FIRST tRNA FLOATS AWAY.



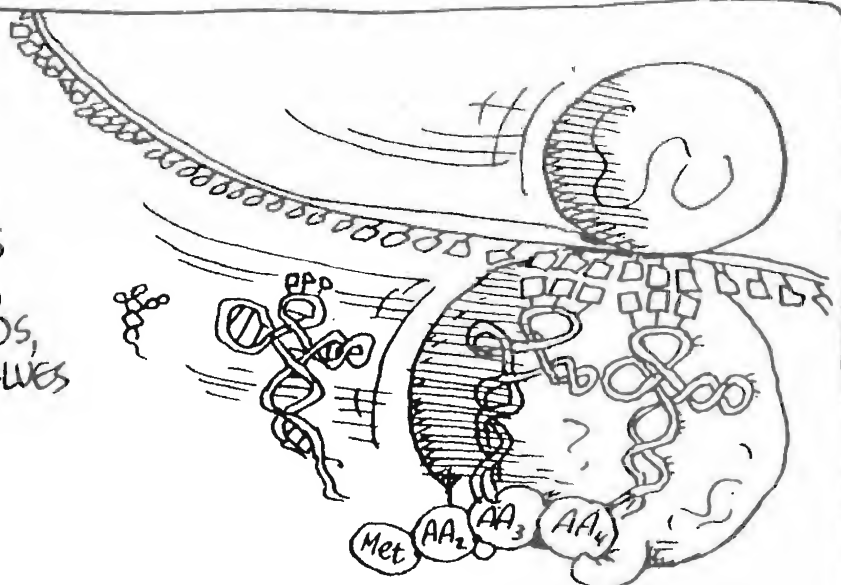
THE RIBOSOME THEN MOVES DOWN THREE MORE BASES.



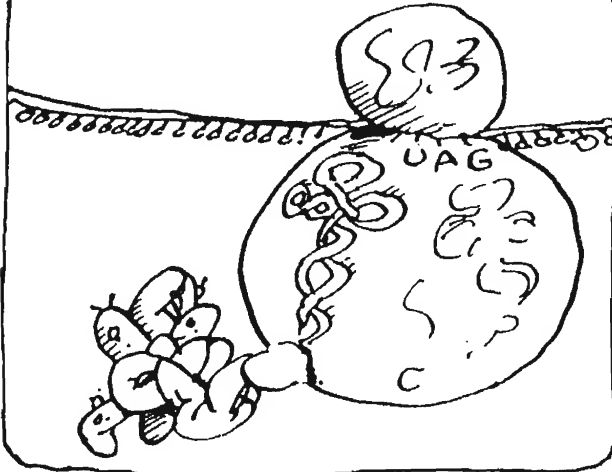
ANOTHER tRNA AND AMINO ACID BIND ON.



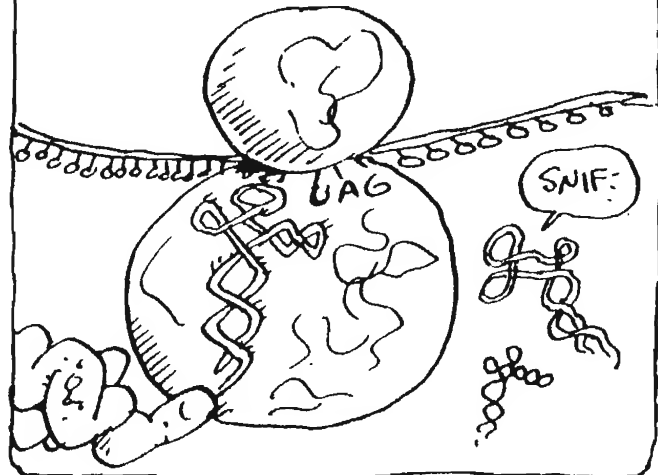
THE AMINO ACIDS ARE LINKED; THE "EMPTY" tRNA IS DISCARDED; AND SO THE RIBOSOME MOVES ALONG THE MESSAGE, PILING UP AMINO ACIDS, WHICH FOLD THEMSELVES INTO A PROTEIN.



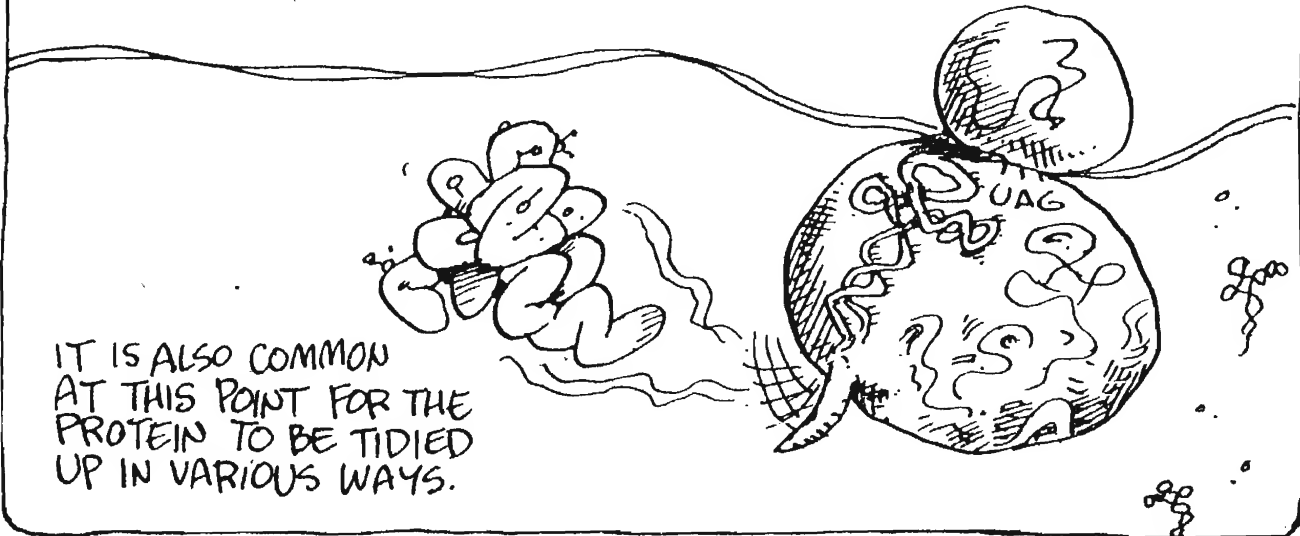
THIS PROCESS CONTINUES UNTIL THE RIBOSOME REACHES ONE OF THE "STOP" SIGNALS.



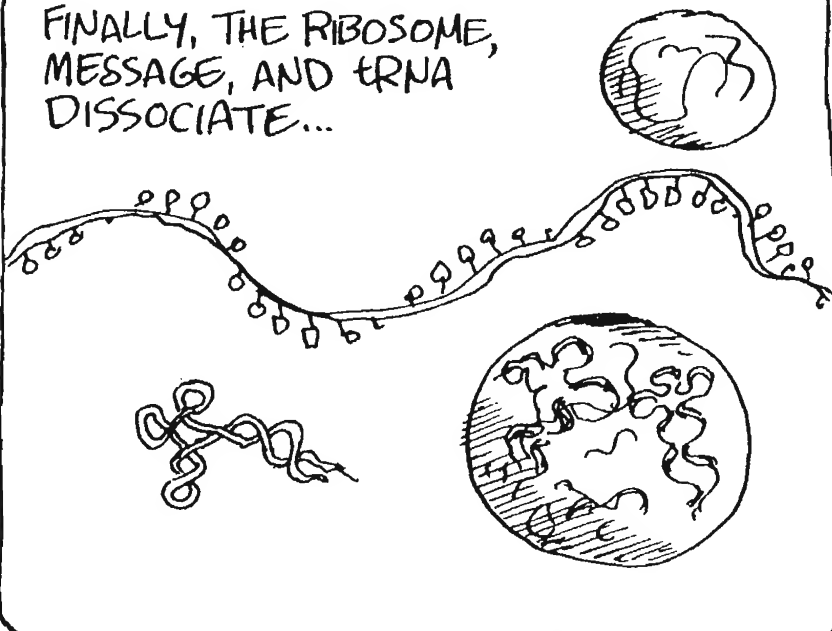
IT STOPS BECAUSE THERE IS NO tRNA WITH AN ANTICODON TO MATCH.



THE COMPLETED PROTEIN IS CLIPPED OFF BY ANOTHER RIBOSOMAL ENZYME.



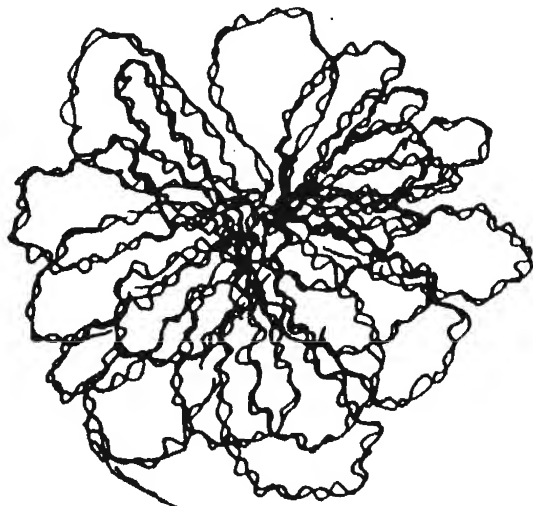
FINALLY, THE RIBOSOME, MESSAGE, AND tRNA DISSOCIATE...



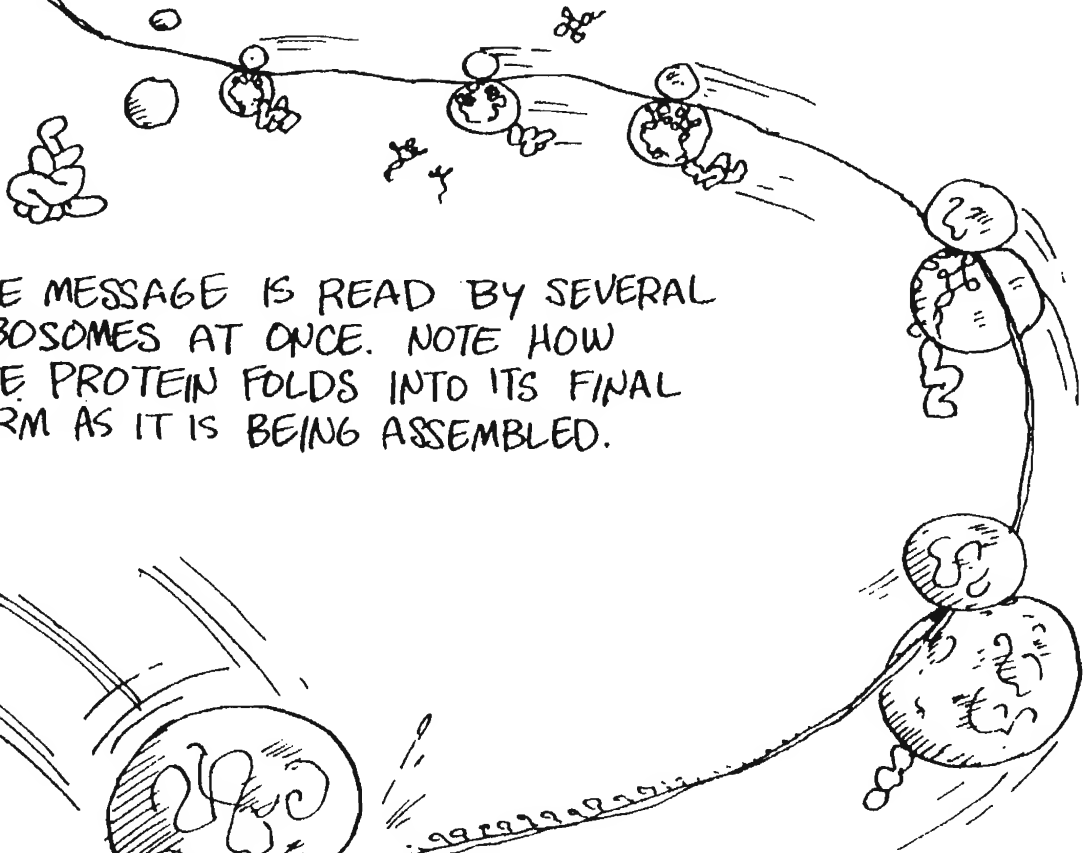
...AND THE NEW MACROMOLECULE GOES OFF TO DO ITS JOB: STRUCTURE, ENZYME, OR WHATEVER...



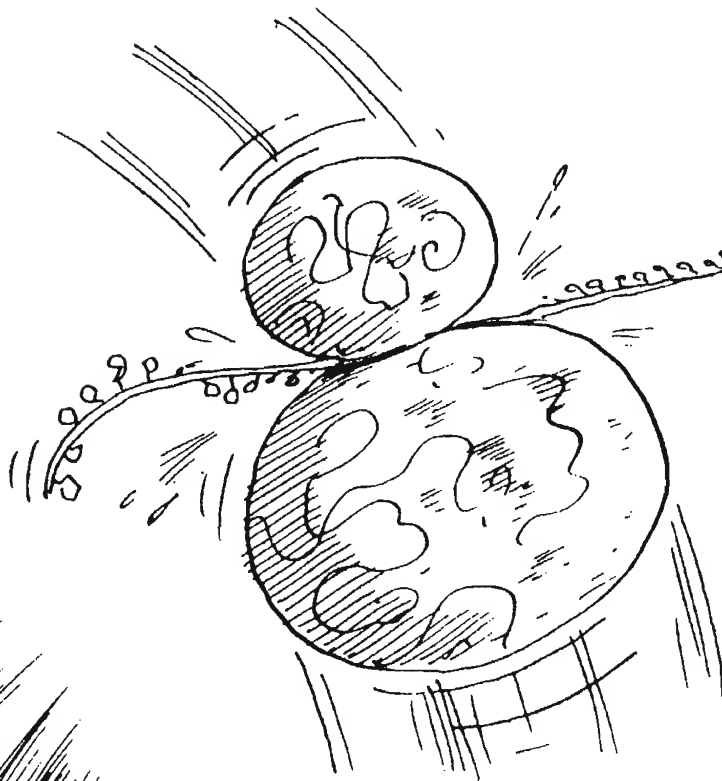
IN THE LIVING CELL, ALL THESE PROCESSES ARE GOING ON TOGETHER. THIS IS HOW IT LOOKS IN *E. COLI*.



IN BACTERIA GENERALLY, PROTEIN-BUILDING BEGINS WHILE THE mRNA IS STILL BEING TRANSCRIBED FROM THE GENE.



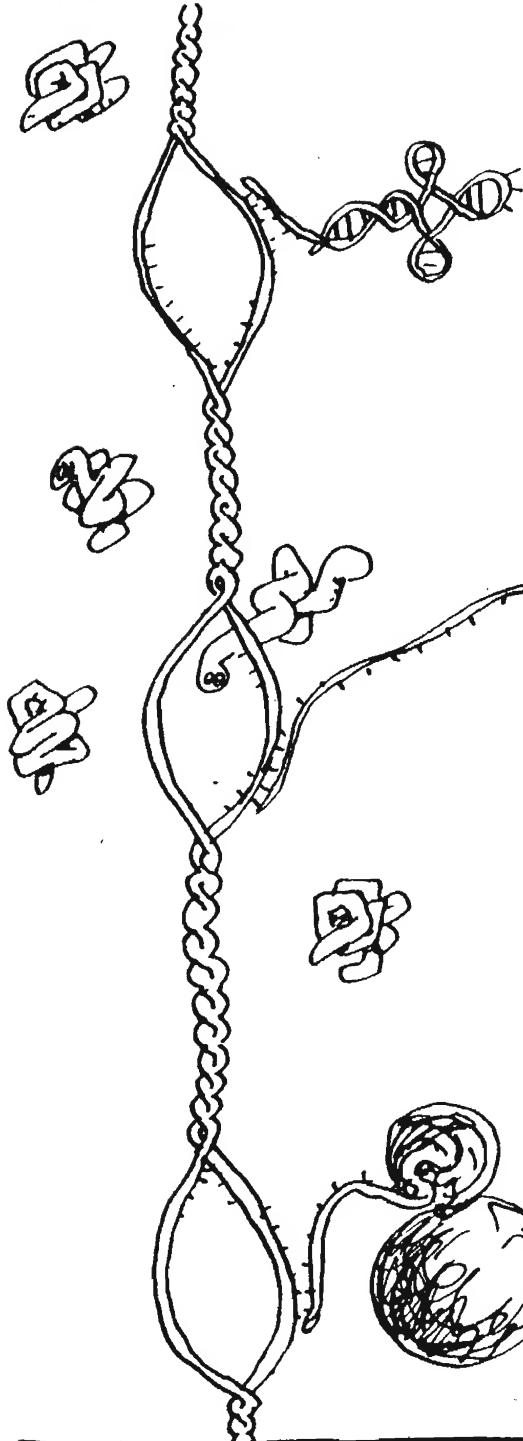
THE MESSAGE IS READ BY SEVERAL RIBOSOMES AT ONCE. NOTE HOW THE PROTEIN FOLDS INTO ITS FINAL FORM AS IT IS BEING ASSEMBLED.



AND NOW YOU UNDERSTAND HOW GENES WORK — IN *E. COLI* !!

NOTE

FOR A MOMENT
HOW MUCH WE'VE
ALREADY FOUND
ENCODED IN THE
CHROMOSOME.



THERE ARE SEQUENCES
ENCODING EVERY
TRANSFER RNA MOLECULE...

...SEQUENCES FOR
mRNA, WHICH ARE
TRANSLATED INTO
PROTEIN...

...AND SEQUENCES
FOR RIBOSOMAL
RNA, WHICH
FITS DIRECTLY
INTO THE
STRUCTURE OF
THE RIBOSOME.

TRULY, THE DNA IS
THE BLUEPRINT OF
ALL THE CELL'S
ESSENTIAL PARTS.

BLUEPRINT?
WHO'S THE
ARCHITECT?



ASK
MENDEL
...

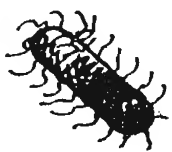
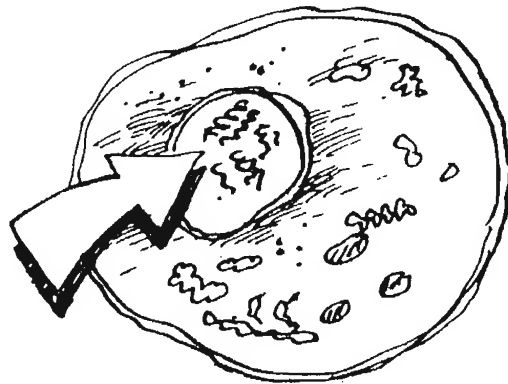
PRO AND EU

WE BEGAN BY ASKING ABOUT GORILLAS AND BANANAS, AND ENDED UP INSIDE SOME INSIGNIFICANT LITTLE BUG, E. COLI... NOW WHAT CAN WE SAY ABOUT OTHER LIFE FORMS?



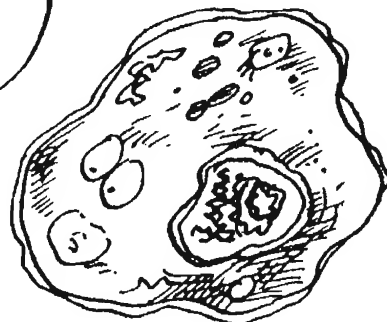
FIRST, SOME MORE JARGON: THE CELLS OF PLANTS, ANIMALS, AND OTHER ADVANCED CREATURES — IN FACT, ANY CELL WITH A NUCLEUS — IS CALLED A EUCARYOTE ("YOU-CARRY-OAT"), MEANING "GOOD NUCLEUS" IN GREEK.

EUCARYOTES CONTAIN ALL SORTS OF BODIES, BUT THE KEY IS THE NUCLEUS, WHICH CONTAINS THE CHROMOSOMES.

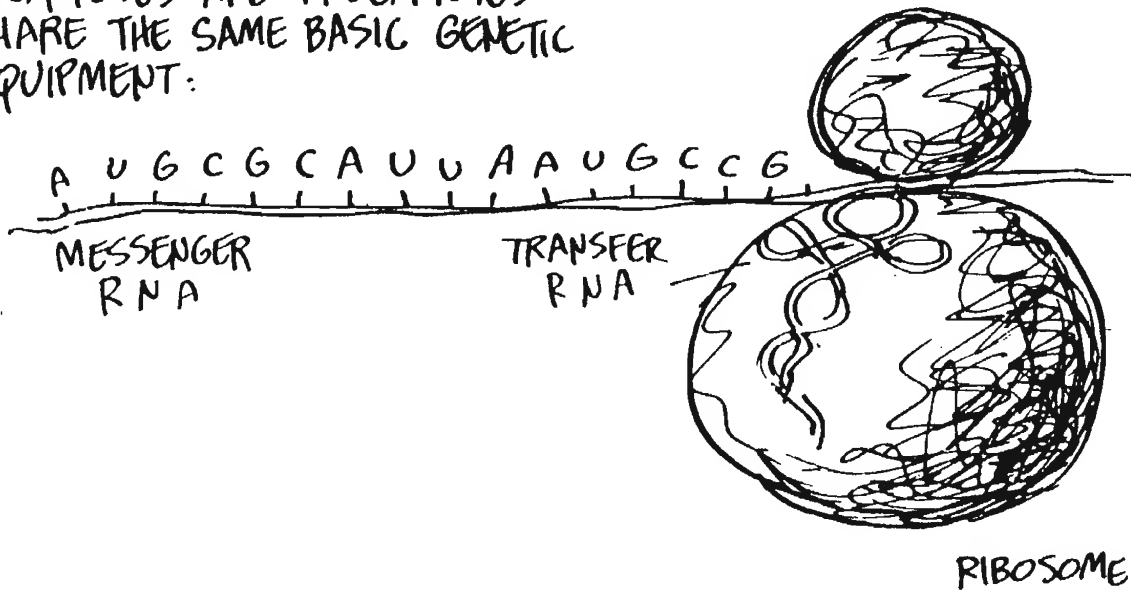


THE TINY BACTERIA, WITH THEIR SIMPLER STRUCTURE, ARE CALLED PROCARYOTES ("PRO-CARRY-OATS"), MEANING "BEFORE NUCLEUS" IN GREEK.

THE IDEA IS THAT PROCARYOTES MUST HAVE EVOLVED BEFORE THE MORE COMPLICATED EUCARYOTES.



EUCARYOTES AND PROCARYOTES
SHARE THE SAME BASIC GENETIC
EQUIPMENT:

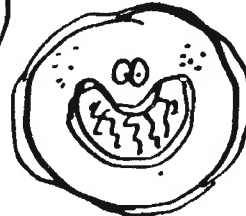


**IN ALL LIFE, THE GENETIC
CODE IS THE SAME —**

A FACT WHICH
STRONGLY SUGGESTS
THAT WE ALL
COME FROM A
COMMON ANCESTOR.

LET'S HAVE
A FAMILY
REUNION
SOMETIME!

ANYTIME...
I'LL BRING
MY GORILLA...

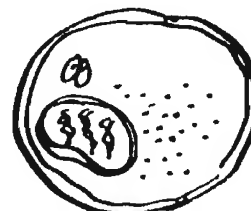


BUT THERE ARE BIG DIFFERENCES BETWEEN PRO
AND EU...

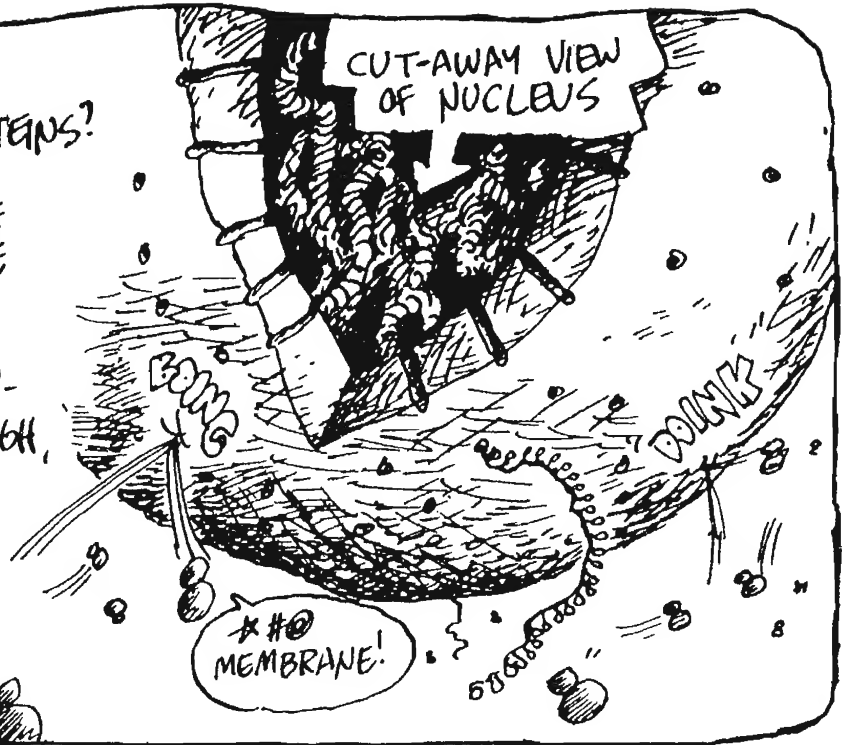
TO BEGIN
WITH, EUCARYOTES
HAVE ALL THEIR
RIBOSOMES
OUTSIDE THE
NUCLEUS, SEPARATED
FROM THE GENES
BY A MEMBRANE.

HOW CAN
YOU MAKE
PROTEINS?

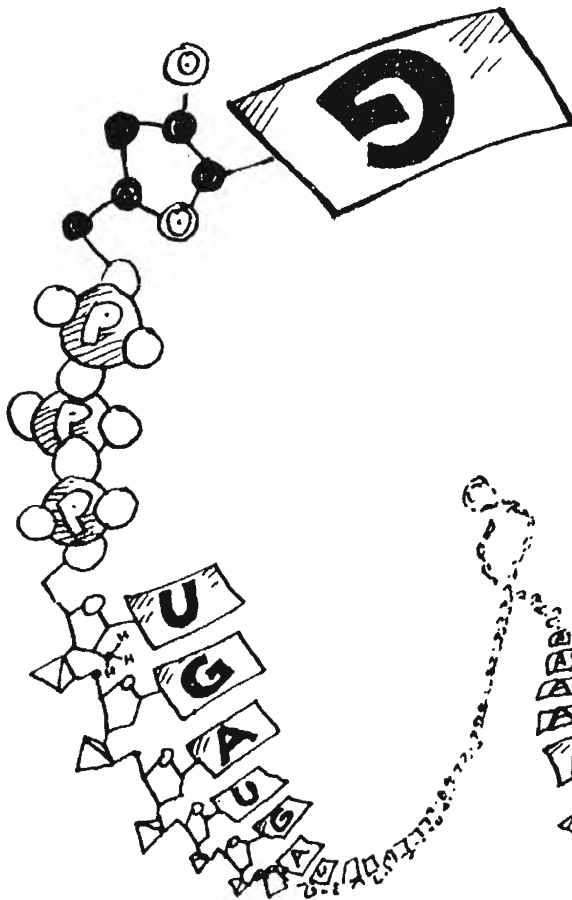
IT'S A BIT
LIKE KISSING
THROUGH PLASTIC...



INDEED, HOW DO EUKARYOTES MAKE PROTEINS? THE ANSWER IS THAT THE NUCLEAR MEMBRANE HAS PORES. THESE ARE BIG ENOUGH TO ALLOW RNA AND VARIOUS ENZYMES, LIKE RNA POLYMERASE, TO PASS THROUGH, BUT RIBOSOMES ARE TOO BIG TO FIT.



WITHIN THE NUCLEUS, mRNA IS MADE AS IN BACTERIA — BUT THEN COME CERTAIN MODIFICATIONS...

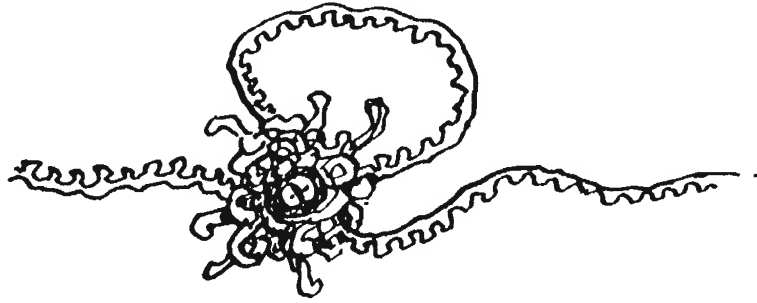


AT THE "START" END IS USUALLY ADDED A MODIFIED, UPSIDE-DOWN **GUANINE** "CAP."

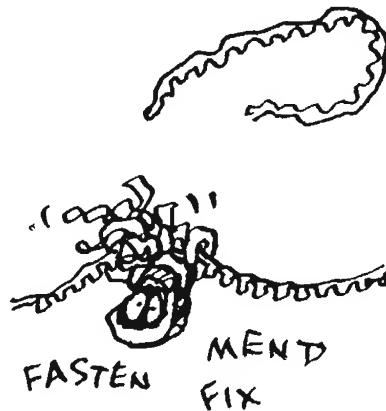
AT THE OTHER END GOES A STRING OF **ADENINE** NUCLEOTIDES, MAKING A **POLY-A TAIL** UP TO SEVERAL HUNDRED NUCLEOTIDES IN LENGTH.

THE FUNCTION OF THESE AND OTHER ADJUSTMENTS TO EUKARYOTIC mRNA IS UNKNOWN.

THE NEXT MOVE CAME AS A GREAT SURPRISE TO GENETICISTS:
A COMPLEX OF PROTEIN AND RNA GRABS THE mRNA, FORMING
LOOPS, LIKE THIS →



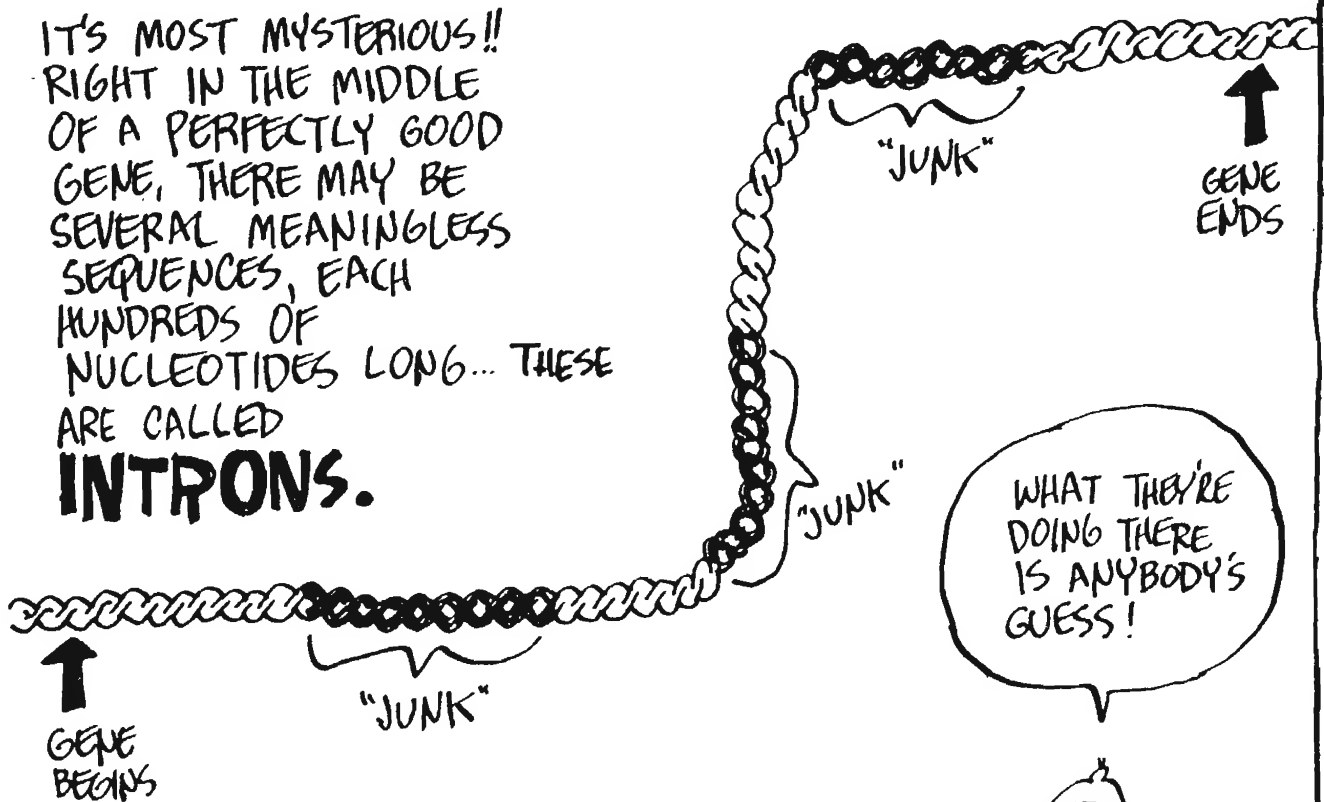
THE COMPLEX — CALLED A **SPICEOSOME** —
THEN SHEARS OFF THE LOOP, DISCARDS IT, SPLICES THE
REMAINING PIECES TOGETHER, AND DEPARTS.



THIS IS BIZARRE! EUKARYOTIC GENES CONTAIN "**JUNK DNA**" —
NON-CODING MESSAGE SEQUENCES THAT HAVE TO BE CUT OUT
BEFORE THE GENE CAN BE EXPRESSED!!



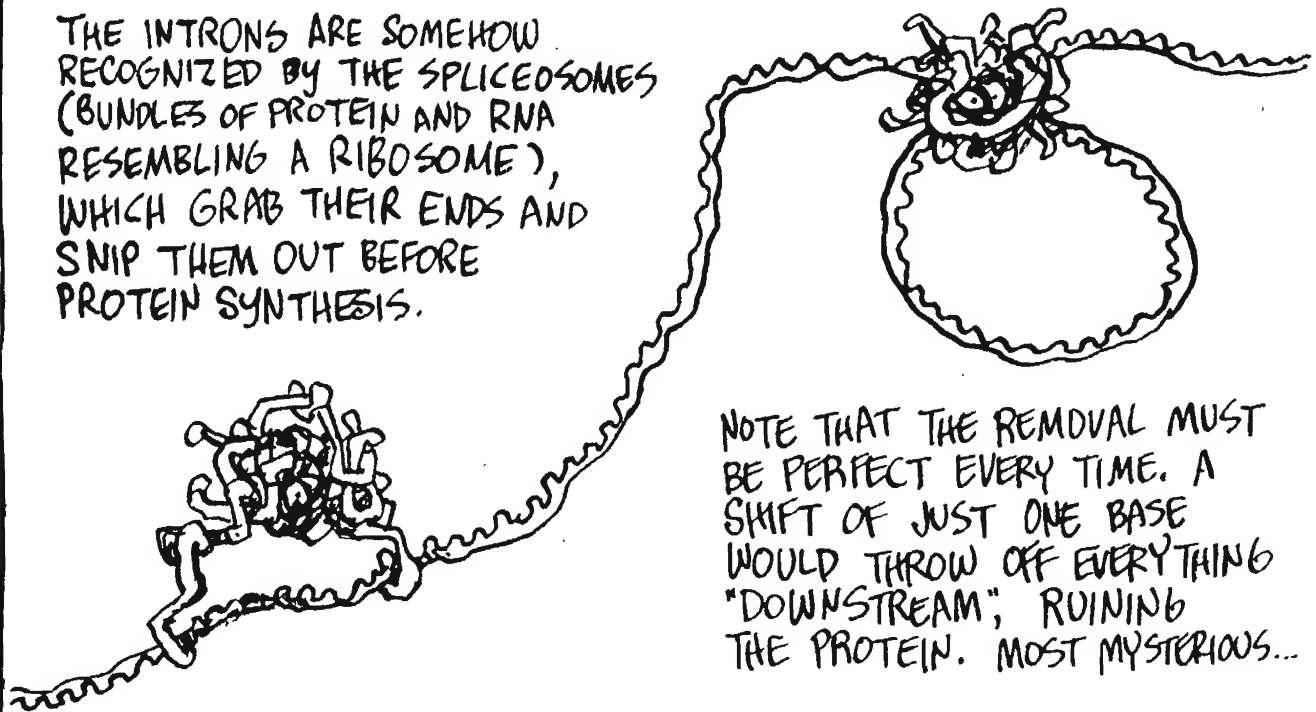
IT'S MOST MYSTERIOUS!!
RIGHT IN THE MIDDLE
OF A PERFECTLY GOOD
GENE, THERE MAY BE
SEVERAL MEANINGLESS
SEQUENCES, EACH
HUNDREDS OF
NUCLEOTIDES LONG... THESE
ARE CALLED
INTRONS.



FOR SOME REASON, EUKARYOTES SEE
FIT TO LEAVE INTRONS IN THE
CHROMOSOME, ONLY REMOVING THEM
FROM mRNA AFTER TRANSCRIPTION.

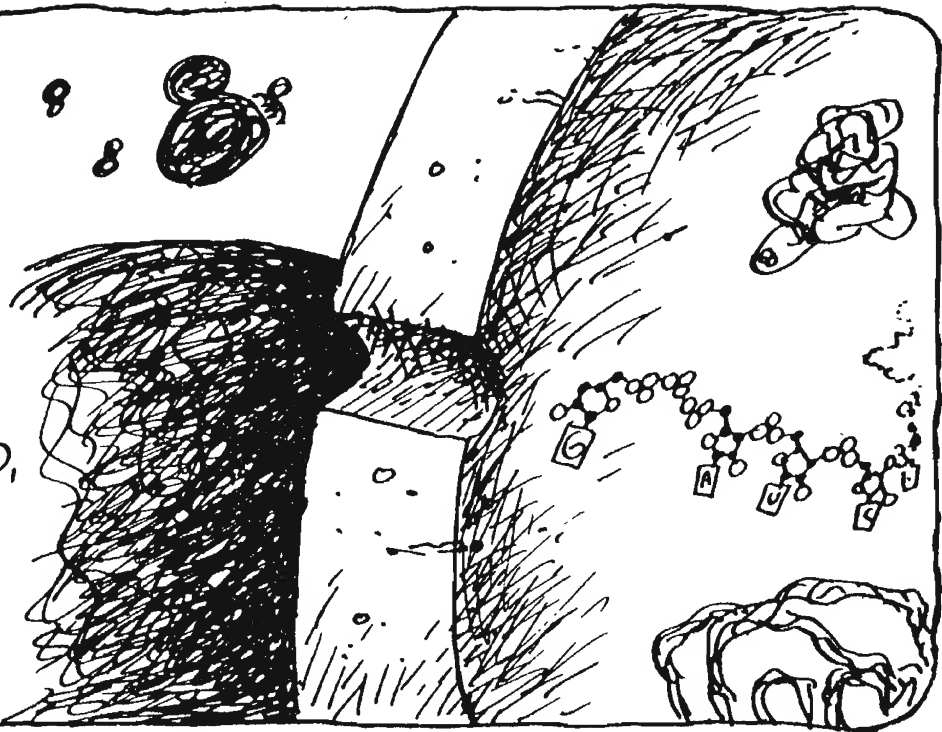


THE INTRONS ARE SOMEHOW
RECOGNIZED BY THE SPLICEOSOMES
(BUNDLES OF PROTEIN AND RNA
RESEMBLING A RIBOSOME),
WHICH GRAB THEIR ENDS AND
SNIP THEM OUT BEFORE
PROTEIN SYNTHESIS.

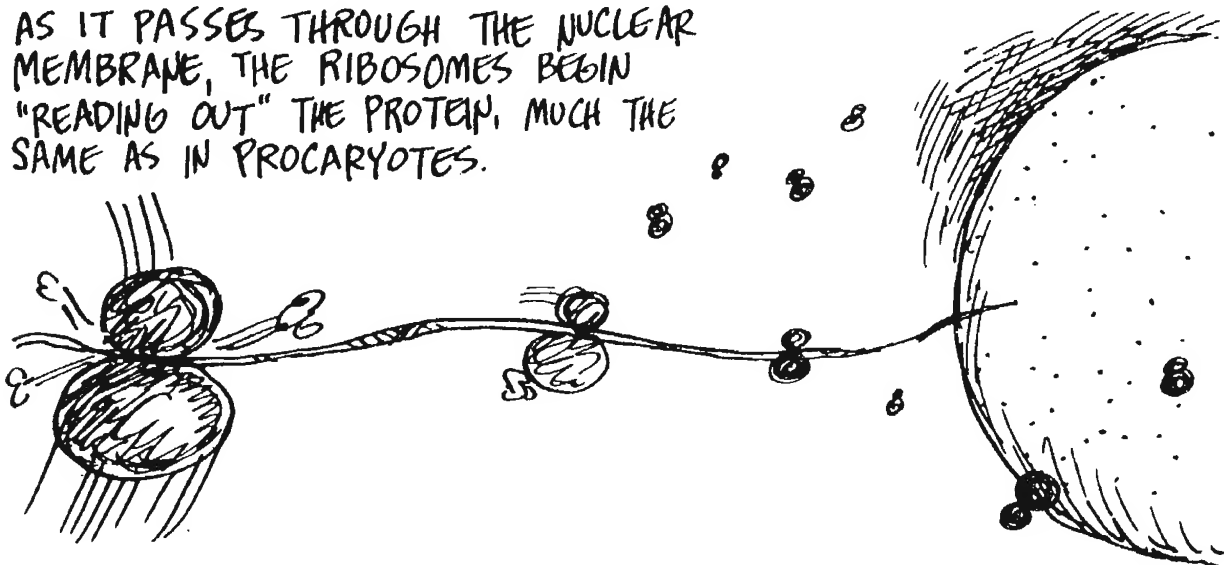


NOTE THAT THE REMOVAL MUST
BE PERFECT EVERY TIME. A
SHIFT OF JUST ONE BASE
WOULD THROW OFF EVERYTHING
"DOWNSTREAM", RUINING
THE PROTEIN. MOST MYSTERIOUS...

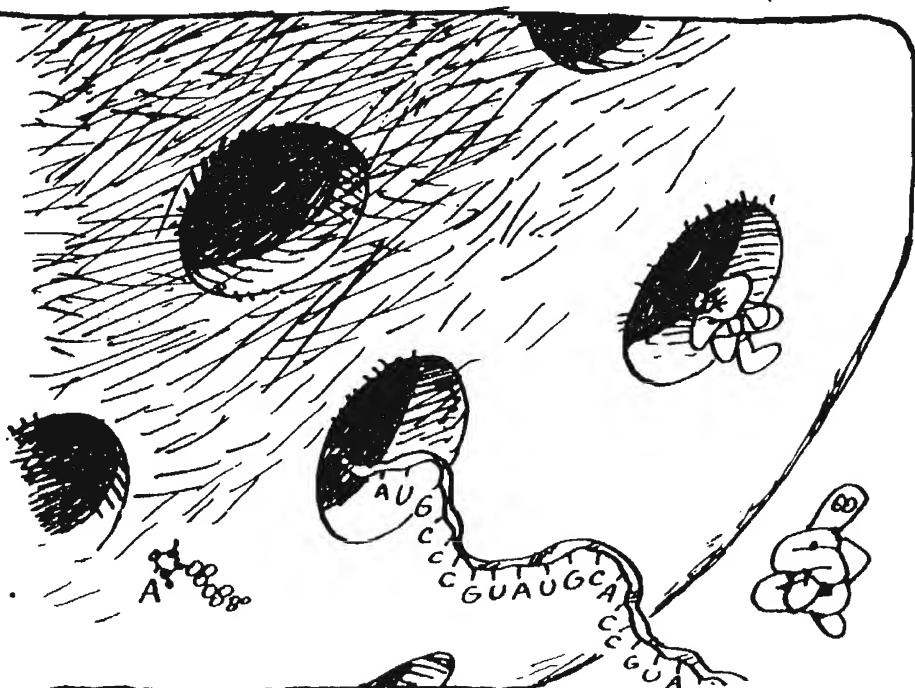
SO FAR,
ALL THIS
ACTION IS
STILL TAKING
PLACE INSIDE
THE NUCLEUS,
BUT NOW THE
MESSENGER,
SUITABLY CAPPED,
TAILED, AND
TRIMMED, IS
READY TO
GO...



AS IT PASSES THROUGH THE NUCLEAR
MEMBRANE, THE RIBOSOMES BEGIN
"READING OUT" THE PROTEIN, MUCH THE
SAME AS IN PROCARYOTES.



FINALLY, THE
PROTEIN GOES OFF
TO DO ITS JOB;
THE mRNA IS
BROKEN DOWN
INTO "SCRAP";
AND THE PARTS
RETURN TO
THE NUCLEUS
FOR RECYCLING,
TOGETHER WITH
THE ENZYMES
THAT DO THE JOB.



ANOTHER

DIFFERENCE BETWEEN EU AND A BACTERIUM IS IN THE SHEER NUMBER OF GENES: 200,000 IN A HUMAN, 4000 IN E. COLI.

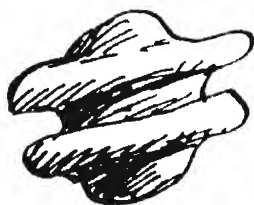


HMM... 200,000 GENES... 1000 NUCLEOTIDES PER GENE... THAT'S 200 MILLION... MY MY!

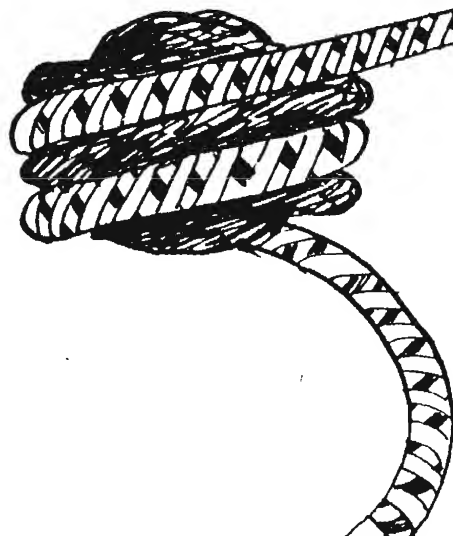
HA! I HAVE THAT MANY SISTERS LIVING IN YOUR GUT!



TO HELP ORGANIZE ALL THAT STORAGE, EUKARYOTES WRAP THEIR DNA AROUND PROTEIN "SPOOLS." EACH "SPOOL"—OR NUCLEOSOME CORE, TO BE PROPER—CONSISTS OF SEVERAL PROTEINS BOUND TOGETHER:

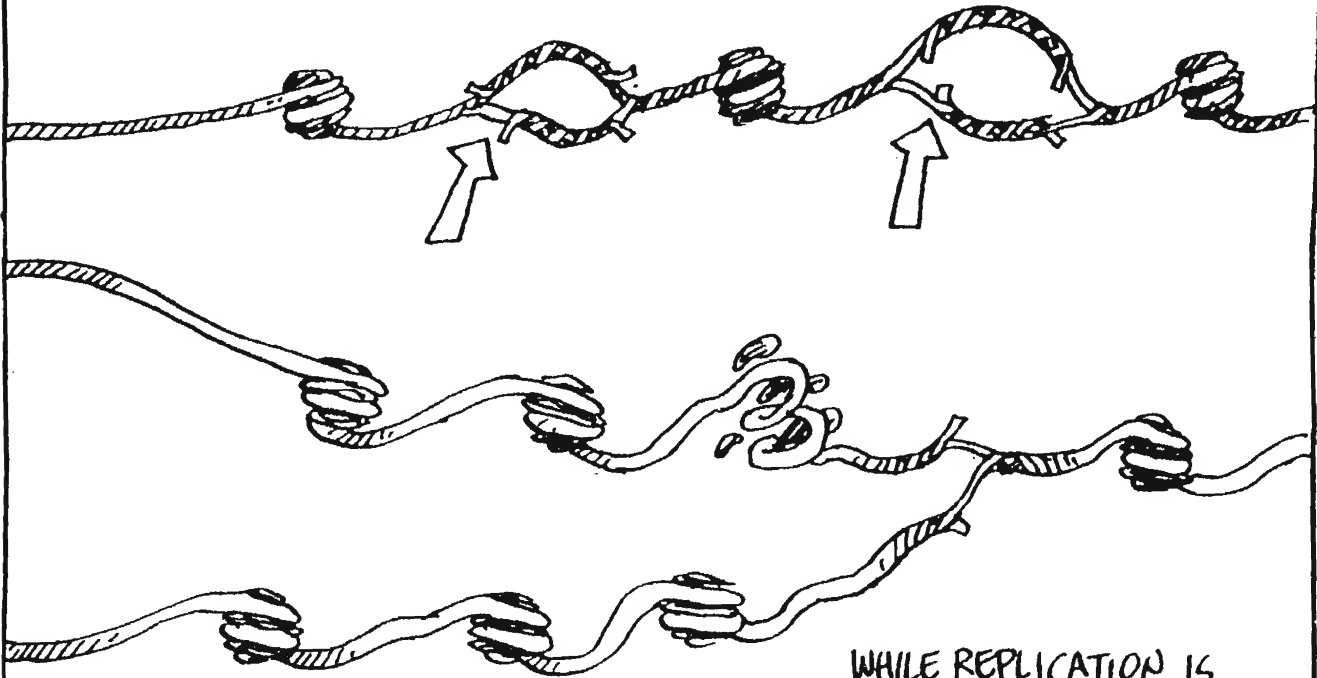


EACH CORE HAS A SPIRAL GROOVE FOR THE DNA, WHICH MAKES TWO TURNS AROUND IT.



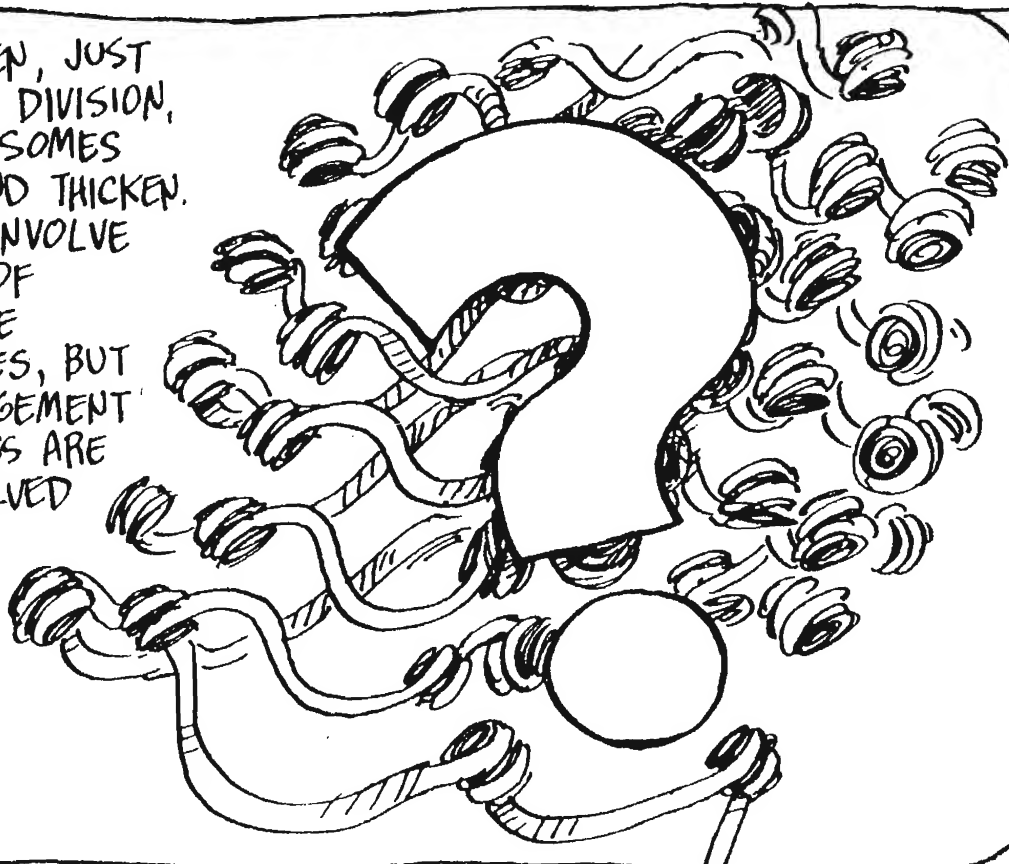
HMM! VERY EXOTIC!

WHEN A EUKARYOTIC CELL WANTS TO DIVIDE, DNA REPLICATION BEGINS AT MANY SITES AT ONCE (UNLIKE IN E. COLI, WHERE IT BEGINS AT ONE SITE).



WHILE REPLICATION IS STILL IN PROGRESS, THE TWO NEW STRANDS ARE ALREADY WINDING ONTO NUCLEOSOME CORES. ONE STRAND INHERITS THE OLD CORES, AND THE OTHER GETS A NEW SET.

AS WE'VE SEEN, JUST BEFORE CELL DIVISION, THE CHROMOSOMES SHORTEN AND THICKEN. THIS MUST INVOLVE SOME WAY OF PACKING THE NUCLEOSOMES, BUT THE ARRANGEMENT AND PROCESS ARE STILL UNSOLVED PROBLEMS.



A THIRD

PECULIARITY
OF EUKARYOTIC GENES: THEY
HARBOR LOTS OF SO-CALLED
REPETITIVE DNA... THESE ARE
SEQUENCES OF NUCLEOTIDES WHICH
REPEAT THEMSELVES MANY TIMES.

WE HUMANS, FOR
EXAMPLE, HAVE ONE
SEQUENCE OF SOME
300 BASE PAIRS
WHICH APPEARS NEARLY
A MILLION TIMES.
THIS IS A SUBSTANTIAL
CHUNK OF OUR TOTAL!
WHAT CAN IT
MEAN ?? !!

A THIRD
PECULIARITY OF
EUKARYOTIC GENES:
THEY HARBOR LOTS
OF SO-CALLED
REPETITIVE DNA.

THESE
ARE SEQUENCES
OF NUCLEOTIDES
WHICH REPEAT
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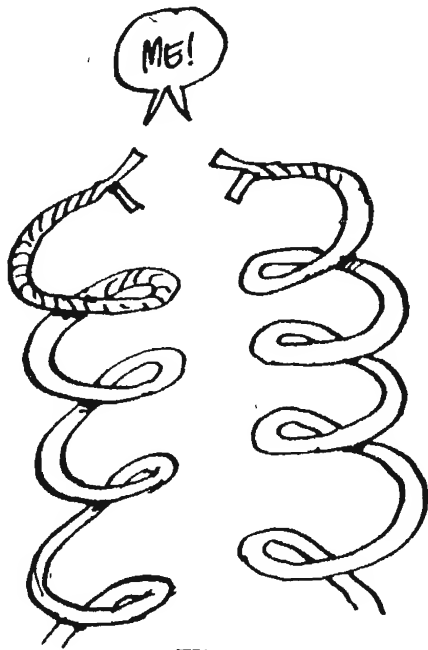
WE HUMANS, FOR
EXAMPLE, HAVE
ONE SEQUENCE OF 300
BASE PAIRS WHICH
APPEARS NEARLY
A MILLION TIMES.

WHAT
CAN IT
MEAN?

THIS IS A
SUBSTANTIAL CHUNK
OF OUR TOTAL!

MAYBE
IT'S ADDED
FOR
EMPHASIS!





A POSSIBLE ANSWER IS THAT THESE SEQUENCES CONSIST OF "**SELFISH DNA**," WHICH CONTRIBUTES NOTHING TO THE ORGANISM. ENCODING NO ENZYMES, IT MAY BE JUST "HITCHING A RIDE" ON OUR CHROMOSOMES!!

A THIRD PECULIARITY OF EUKARYOTIC GENES: THEY HARBOR LOTS OF SO-CALLED REPETITIVE DNA.

THESE ARE SEQUENCES OF NUCLEOTIDES WHICH REPEAT THEMSELVES MANY TIMES..

O.K! O.K!
I GET THE IDEA !!!

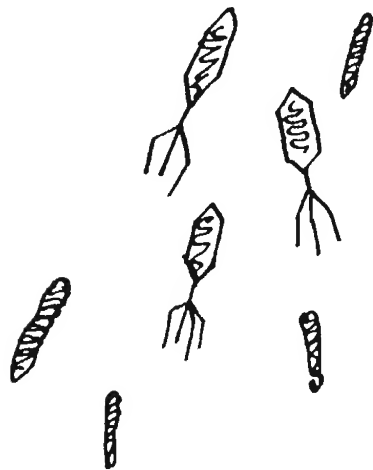


GOIN' TO KANSAS CITY?

WHERE MIGHT THESE GENETIC HITCHHIKERS COME FROM?

ONE POSSIBILITY IS
THAT THEY COME FROM

VIRUSES

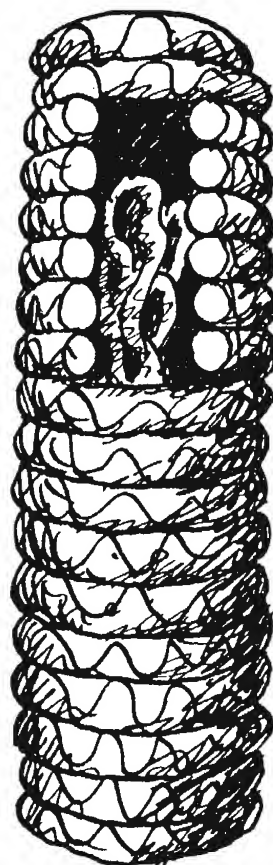


VIRUSES ARE THE SIMPLEST
LIVING THINGS KNOWN—
IF THEY'RE TRULY ALIVE AT
ALL... THEY'RE SORT OF
ALIVE AND NOT ALIVE...



REMINDS
ME OF MY
OLD
BIOLOGY
TEACHER...

EVEN SIMPLER AND SMALLER
THAN A BACTERIUM, A
VIRUS HAS ONLY TWO PARTS:
A BIT OF NUCLEIC ACID
WRAPPED UP IN A PROTEIN
COAT:



CUT-AWAY
VIEW

THE NUCLEIC
ACID, WHICH
MAY BE DNA
OR RNA,
ENCODES THE
PROTEIN COAT
AND A FEW
ENZYMES
NEEDED FOR
REPLICATION.

BUT A VIRUS
CAN'T REPRODUCE
ON ITS OWN,
BECAUSE IT LACKS
RIBOSOMES AND
THE REST OF
A LIVING CELL'S
PROTEIN-MAKING
EQUIPMENT.
A VIRUS CAN
ONLY "LIVE" AS A
PARASITE, BY
INVADING A
HOST CELL
AND TAKING OVER
ITS RIBOSOMES,
ENZYMES, AND
ENERGY.

VIRUSES
LANDING ON
A BACTERIUM,
INJECTING
IT WITH
VIRAL DNA

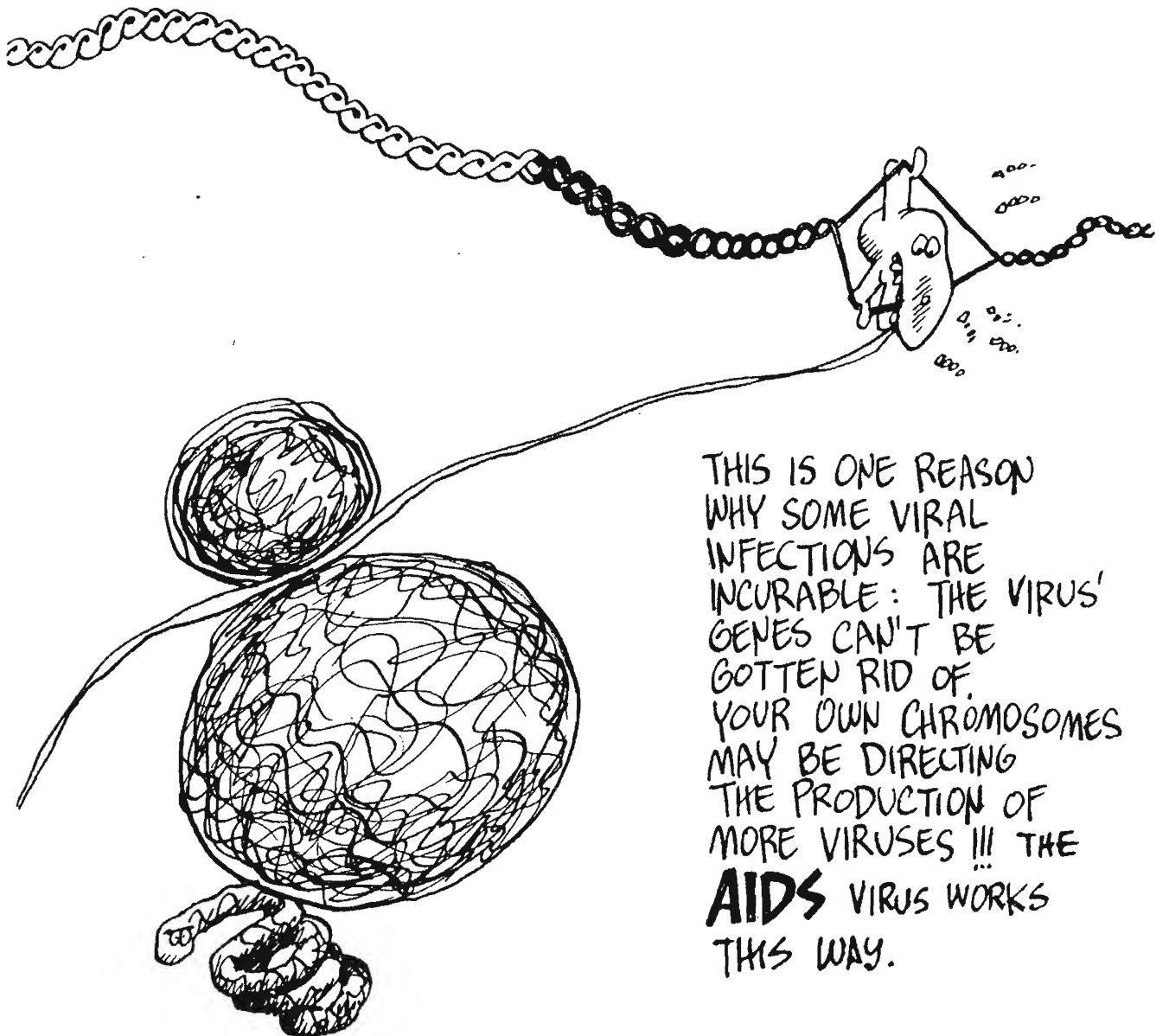
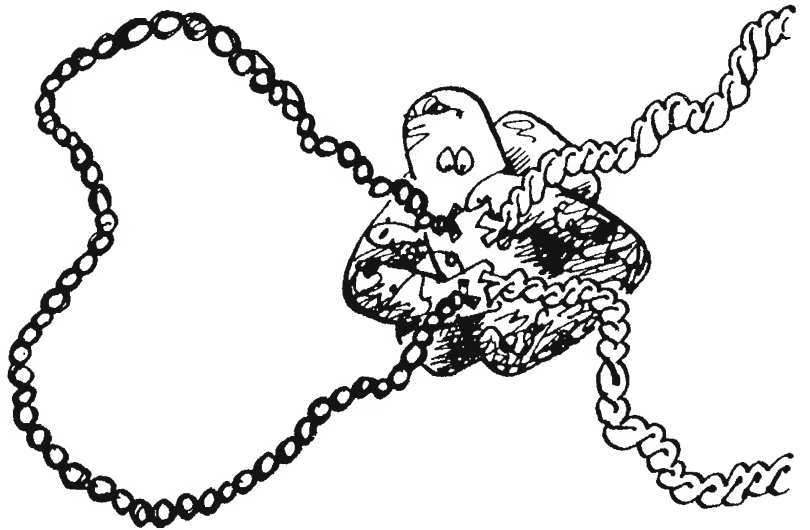


ONCE IT GETS ITS DNA OR RNA INTO THE HOST, THE
VIRUS BEGINS TO REPRODUCE WILDLY, STRAINING THE
CELL TO THE BURSTING POINT!



THAT'S A TYPICAL LIFE-STYLE (OR NON-LIFE-STYLE) FOR A VIRUS, BUT SOME VIRUSES ARE EVEN SNEAKIER: THEY ACTUALLY INSERT THEIR GENES INTO THE HOST CELL'S DNA.

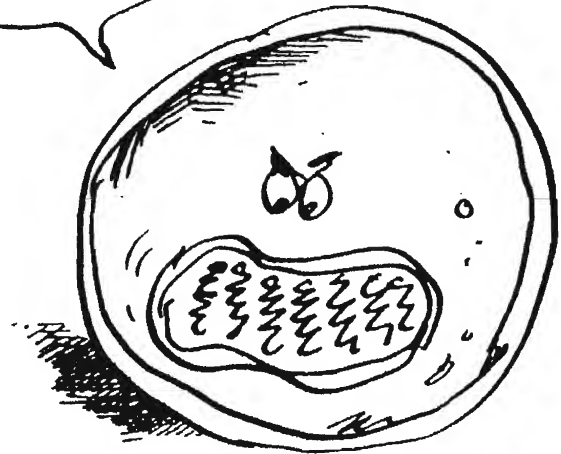
A **RETRO-VIRUS** IS AN RNA VIRUS ENCODING AN ENZYME THAT MAKES A DNA COPY OF ITS RNA AND SPLICES IT INTO THE HOST CHROMOSOME.



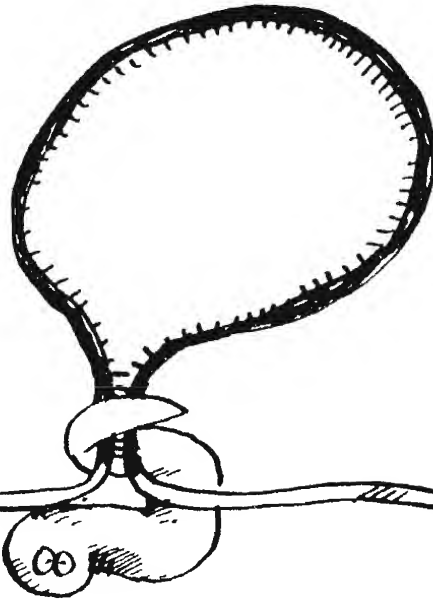
THIS IS ONE REASON WHY SOME VIRAL INFECTIONS ARE INCURABLE: THE VIRUS' GENES CAN'T BE GOTTEN RID OF. YOUR OWN CHROMOSOMES MAY BE DIRECTING THE PRODUCTION OF MORE VIRUSES !!! THE **AIDS** VIRUS WORKS THIS WAY.

IT'S POSSIBLE THAT SOME OF THE REPETITIVE AND "JUNK" DNA IN OUR CHROMOSOMES MAY HAVE COME FROM THIS SOURCE: ANCIENT VIRUSES THAT MANAGED TO INSERT THEIR HEREDITARY BLUEPRINT INTO OUR ANCESTORS' DNA.

SUBVERSIVE ELEMENTS!

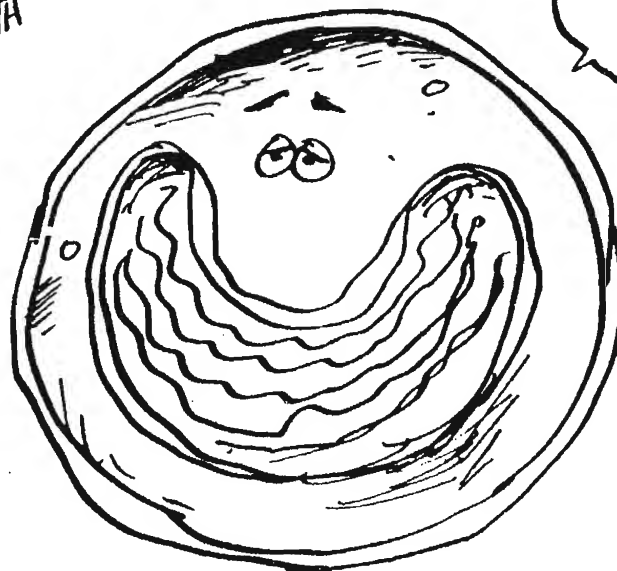


IF SO, THE "EDITING" OF mRNA MAY HAVE EVOLVED AS A DEFENSE AGAINST INAPPROPRIATE SEQUENCES STUCK INTO THE MIDDLE OF GENES.



THERE'S ANOTHER WAY A CELL CAN CONTEND WITH PARASITIC DNA: IT CAN SIMPLY SHUT THOSE GENES DOWN. THAT'S HOW WE DEAL WITH REPETITIVE SEQUENCES: THEY'RE THERE, BUT WE IGNORE THEM!

IT'S CALLED "REPRESSIVE TOLERANCE."



THE BATTLE AGAINST VIRUSES IS NEVER-ENDING...

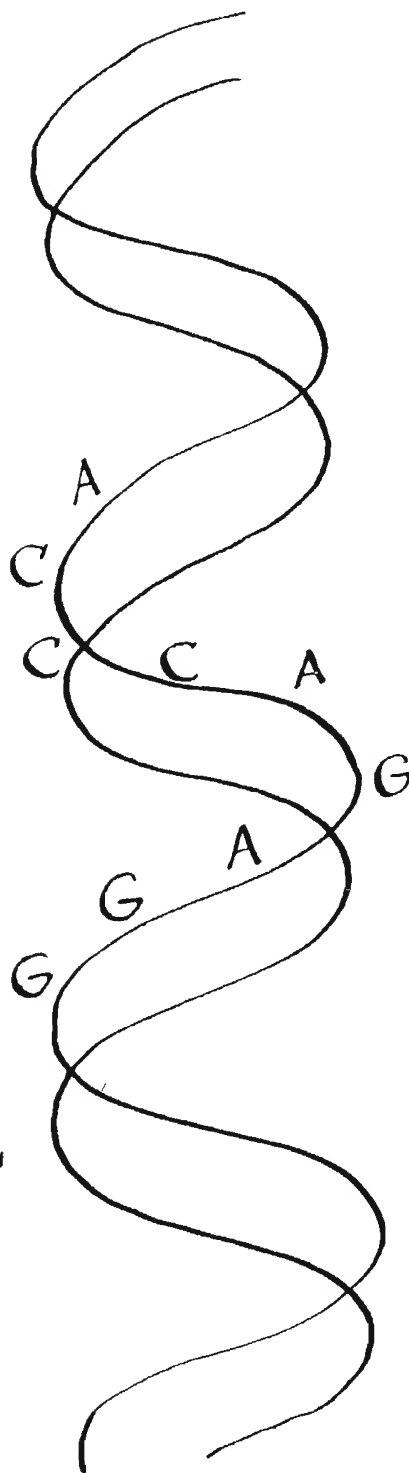
Mutation & Dominance

(again!)

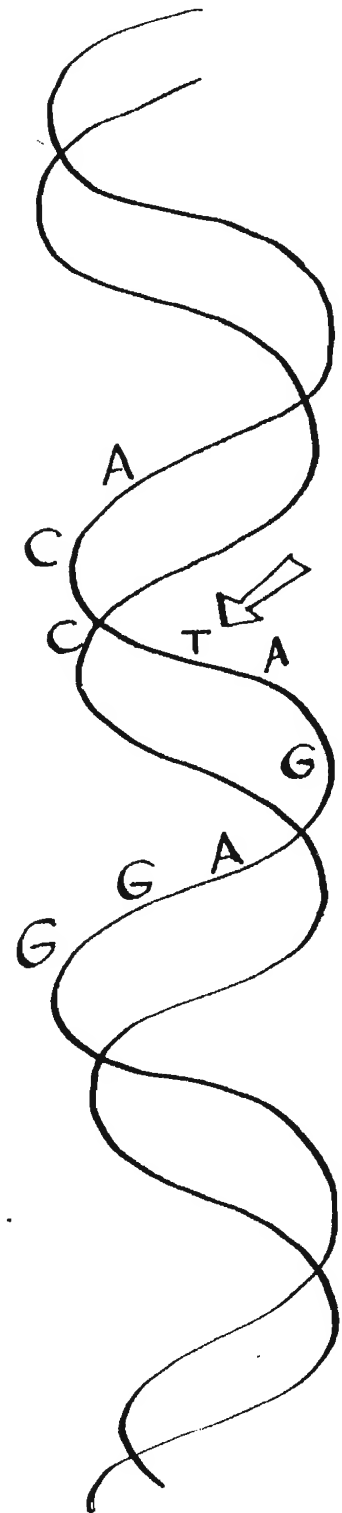
NOW THAT WE KNOW WHAT GENES REALLY ARE, WE CAN GET A MUCH BETTER GRASP OF **MUTATION AND DOMINANCE.**

A MUTATION IN A GENE IS JUST A CHANGE IN THE DNA'S SEQUENCE OF NUCLEOTIDES. EVEN A MISTAKE AT JUST **ONE POSITION** CAN HAVE A PROFOUND EFFECT.

HERE IS A SMALL BUT DEVASTATING MUTATION IN THE GENE FOR **HEMOGLOBIN**, THE PROTEIN WHICH CARRIES OXYGEN IN THE BLOOD.

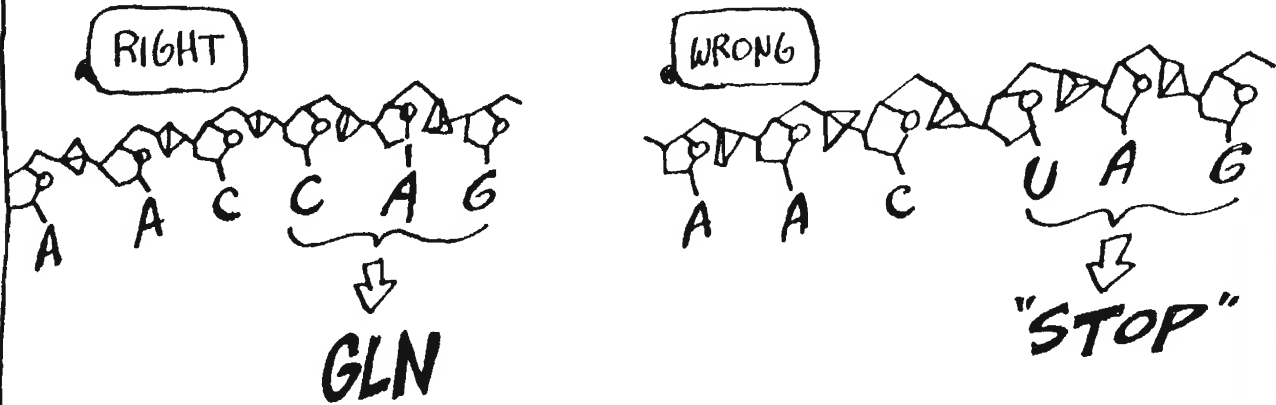


GOOD GENE



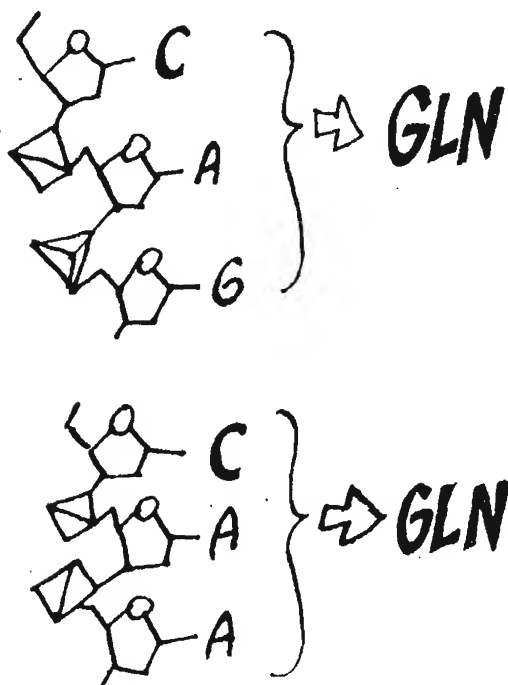
MUTANT GENE

THE REASON, OF COURSE, IS THAT THE CHANGE IS REFLECTED IN THE **PROTEIN** WHICH THE GENE ENCODES... FIRST THE mRNA COMES OUT WRONG, AND THEN THE PROTEIN...



THIS ESPECIALLY DASTROUS MUTATION, WHICH INTERRUPTS THE PROTEIN IN THE MIDDLE, CAUSES A SERIOUS CONDITION CALLED **THALASSEMIA**, AN INABILITY TO MAKE HEMOGLOBIN. THE VICTIM SUFFERS FROM A PAINFUL LACK OF OXYGEN.

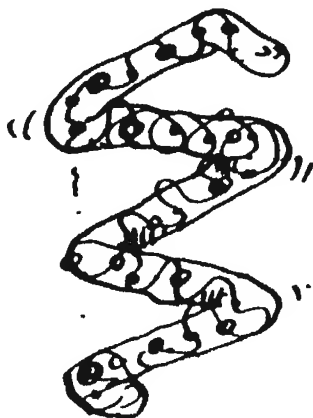
SOMETIMES A CHANGE MAY MAKE NO DIFFERENCE AT ALL. IF YOU REFER BACK TO THE CODE TABLE, YOU'LL RECALL THAT IT'S SOMEWHAT **REDUNDANT** — MEANING THAT ONE AMINO ACID MAY BE ENCODED BY SEVERAL DIFFERENT CODONS.



OCCASIONALLY, THE "MISTAKEN" AMINO ACID MAY FIT IN FAIRLY WELL (THOUGH USUALLY LESS THAN PERFECTLY).



SOMETIMES — ONCE IN A BLUE MOON — THE PROTEIN MAY EVEN WORK **BETTER** THAN BEFORE.



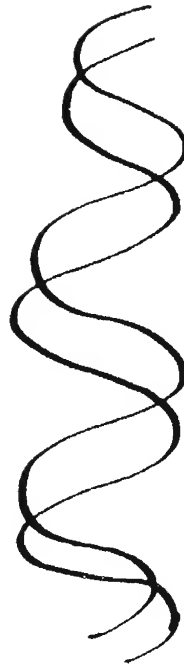
BUT MOST OF THE TIME, A MUTATION JUST RUINS THE PROTEIN. IT'S MUCH EASIER TO MESS SOMETHING UP THAN TO IMPROVE IT! IF YOU DOUBT IT, TRY MAKING RANDOM CHANGES IN SOME HOUSEHOLD APPLIANCE!!



EARLIER (p. 81)

WE NOTED THAT MOST MUTATIONS ARE **RECESSIVE**. NOW WE CAN SEE WHY:
A MUTATION USUALLY CAUSES AN **INABILITY** TO MAKE AN ENZYME. IN THE EXAMPLE ABOVE, THE MUTANT GENE FAILED TO MAKE HEMOGLOBIN.

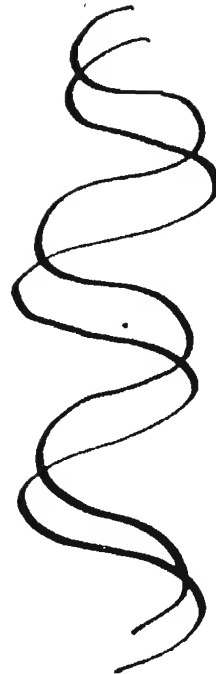
HOWEVER, WE HAVE TWO SETS OF CHROMOSOMES. EVEN IF A MUTATION AFFECTS ONE OF THEM, THE "INSURANCE" GENE WILL STILL PRODUCE ITS ENZYME.



GOOD GENE



HEMOGLOBIN



BAD GENE



NO HEMOGLOBIN

ONLY THE UNLUCKY SOUL WITH A DOUBLE DOSE OF MUTANT GENES WILL BE AFFLICTED WITH THALASSEMIA.



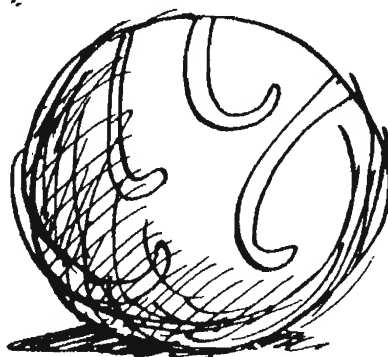
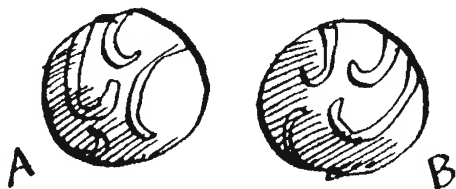
WE DIDN'T MENTION IT
EARLIER, BUT SOME ALLELES
CAN BE

CO- DOMINANT,

MEANING THAT A
HETEROZYGOTE MAKES
BOTH PHENOTYPES.
AN EXAMPLE IS BLOOD
GROUPS.



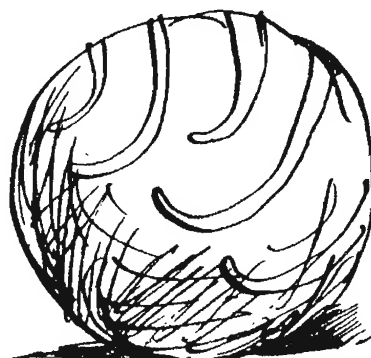
THERE IS A GENETICALLY
DETERMINED SEQUENCE
OF SUGARS LYING ON THE
SURFACE OF RED BLOOD
CELLS. ONE ALLELE, I^A ,
MAKES SEQUENCE A.
ANOTHER ALLELE, I^B ,
MAKES SEQUENCE B.



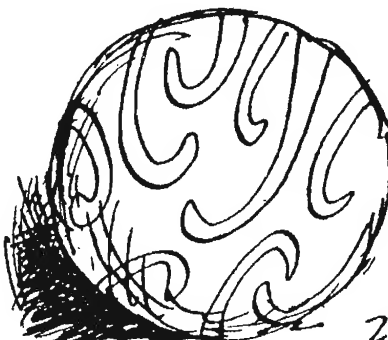
$I^A I^A$

IF HOMOZYGOUS FOR
 I^A , YOUR BLOOD HAS
ONLY SEQUENCE A.
THIS IS TYPE A BLOOD.

$I^B I^B$

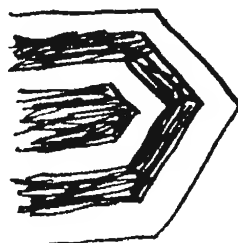


IF HOMOZYGOUS FOR
 I^B , YOU HAVE TYPE B
BLOOD.



$I^A I^B$

A HETERO-
ZYGOTE MAKES
BOTH SEQUENCES,
AND HAS TYPE AB
BLOOD.



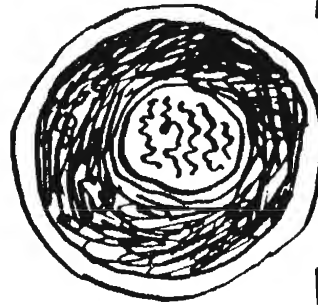
AND FINALLY, THERE
IS A THIRD
ALLELE, I^O , MAKING
NO SUGAR
SEQUENCE.
TYPE O BLOOD IS
RECESSIVE.



BLOOD CELLS ILLUSTRATE
ANOTHER COMMON
FACT OF LIFE:
ONE KIND OF
CELL CAN TURN
INTO ANOTHER
KIND OF CELL.



A RED BLOOD CELL BEGINS
ITS EXISTENCE AS A BONE
MARROW CELL,
A PERFECTLY
GOOD
EUCARYOTE,
BUT
LACKING IN
HEMOGLOBIN.

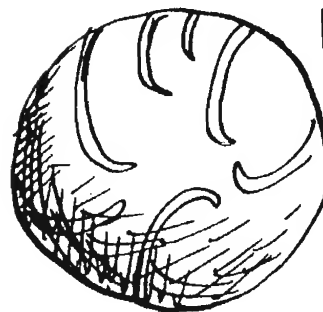


AT SOME POINT,
A MARROW CELL
BEGINS TO
CHANGE...
AMONG
OTHER
THINGS, IT
BEGINS TO
MAKE HEMOGLOBIN.



EVENTUALLY, IT
EMERGES AS A

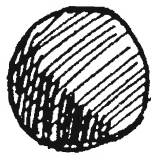
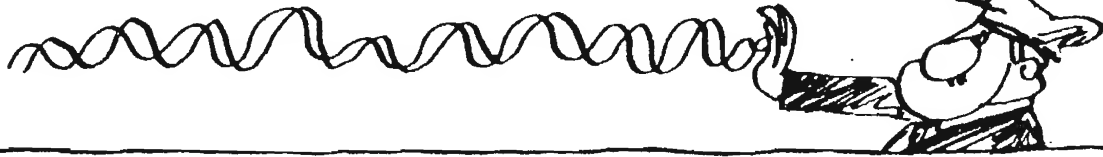
FULLY
DEVELOPED
RED BLOOD
CELL.



GENETICALLY,
THE POINT IS THIS: THE
HEMOGLOBIN GENE
WAS THERE ALL THE
TIME, BUT IT WASN'T
ALWAYS EXPRESSED—
WHICH BRINGS US TO
OUR NEXT SUBJECT...

GENE REGULATION

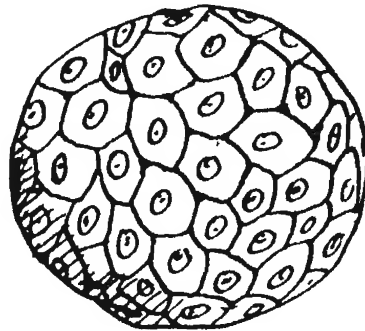
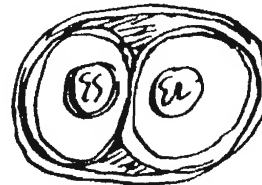
SORRY-
YOU CAN'T
PARK THAT
GENE HERE-



ALL THE HIGHER LIFE
FORMS EXHIBIT AN
IMPRESSIVE COLLECTION OF
CELL TYPES: NERVE,
BLOOD, MUSCLE, SKIN, EYE,
LYMPH, ETC ETC ETC...

BUT

DESPITE THEIR
DIFFERENCES,
ALL THESE
CELLS HAVE
PRECISELY
THE SAME
SET OF GENES*,
BECAUSE
THEY ARISE
FROM ONE
FERTILIZED
EGG BY
THE PROCESS
OF MITOSIS,
WHICH
DUPLICATES
THE
CHROMOSOMES.



*AS USUAL, THERE ARE EXCEPTIONS!!

CLEARLY, DIFFERENT
GENES COME
INTO PLAY
IN DIFFERENT
CELLS... SO
EACH CELL MUST
HAVE WAYS
OF "DECIDING"
WHICH GENES
TO "TURN ON"
AND WHEN
TO DO IT...



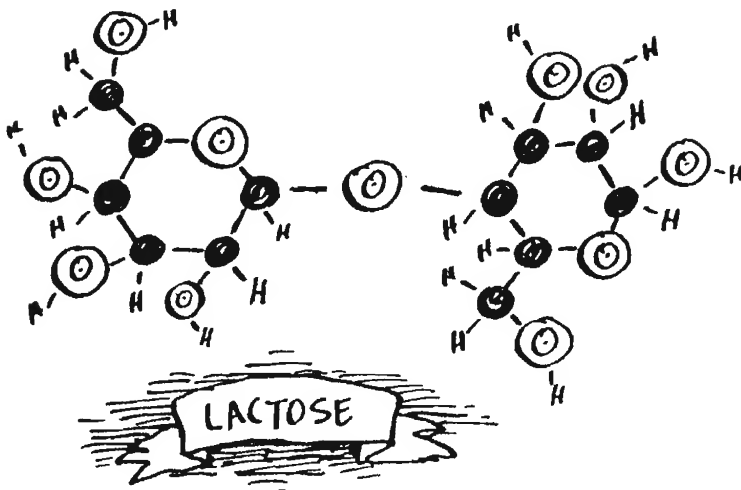
OTHERWISE,
ONE DREADS
THE RESULTS!

EVEN THE LOWLY BACTERIUM NEEDS TO REGULATE ITS GENES.
WHEN FOOD IS AVAILABLE, IT NEEDS TO MAKE ENZYMES TO
DIGEST IT; WHEN IT RUNS LOW ON AN AMINO ACID, IT HAS
TO SYNTHESIZE MORE; ETC ETC ETC...

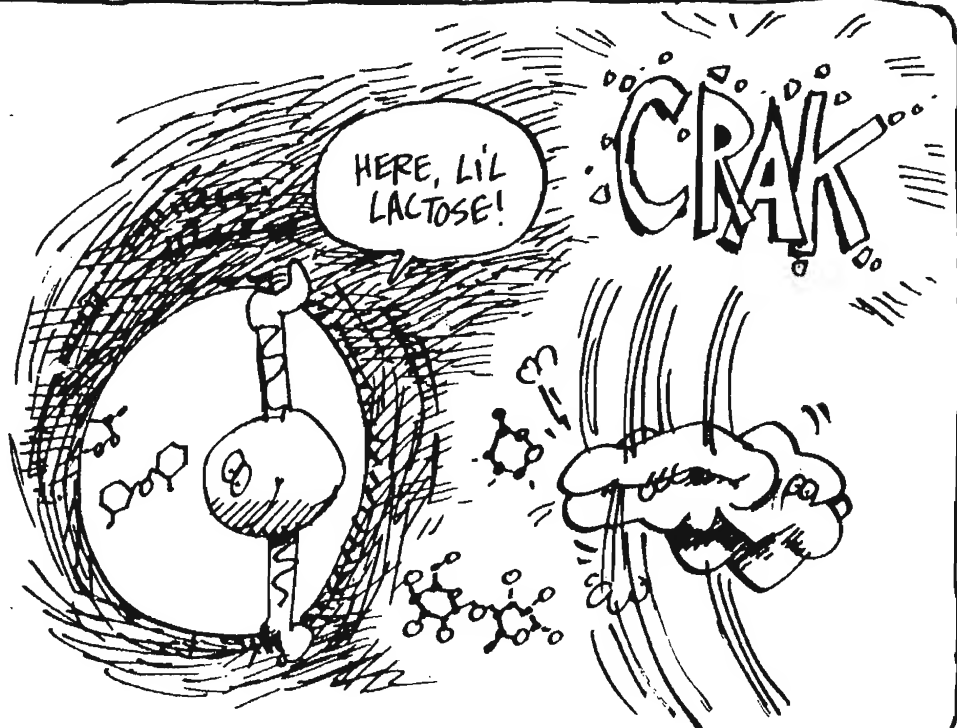


AS USUAL,
THE QUESTION
HAS BEEN
MOST THOROUGHLY
STUDIED IN
E. COLI.

THE FIRST TO FIND A FORM OF GENE REGULATION WERE THE FRENCH SCIENTISTS JACQUES MONOD AND FRANÇOIS JACOB, IN THE LATE 1950'S. THEY EXAMINED *E. COLI*'S ABILITY TO DIGEST THE SUGAR LACTOSE.



IN THE PRESENCE OF LACTOSE, *E. COLI* PRODUCES TWO ENZYMES, CALL THEM Y AND Z*. Z OPENS THE CELL WALL TO LACTOSE, AND Y BREAKS THE SUGAR IN HALF.



* REAL NAMES: BETA-GALACTOSIDASE AND PERMEASE, RESPECTIVELY

WITHOUT GOING INTO THE DETAILS OF THEIR EXPERIMENTS, WHICH WERE QUITE INVOLVED, HERE ARE SOME OF MONOD AND JACOB'S MAIN RESULTS:

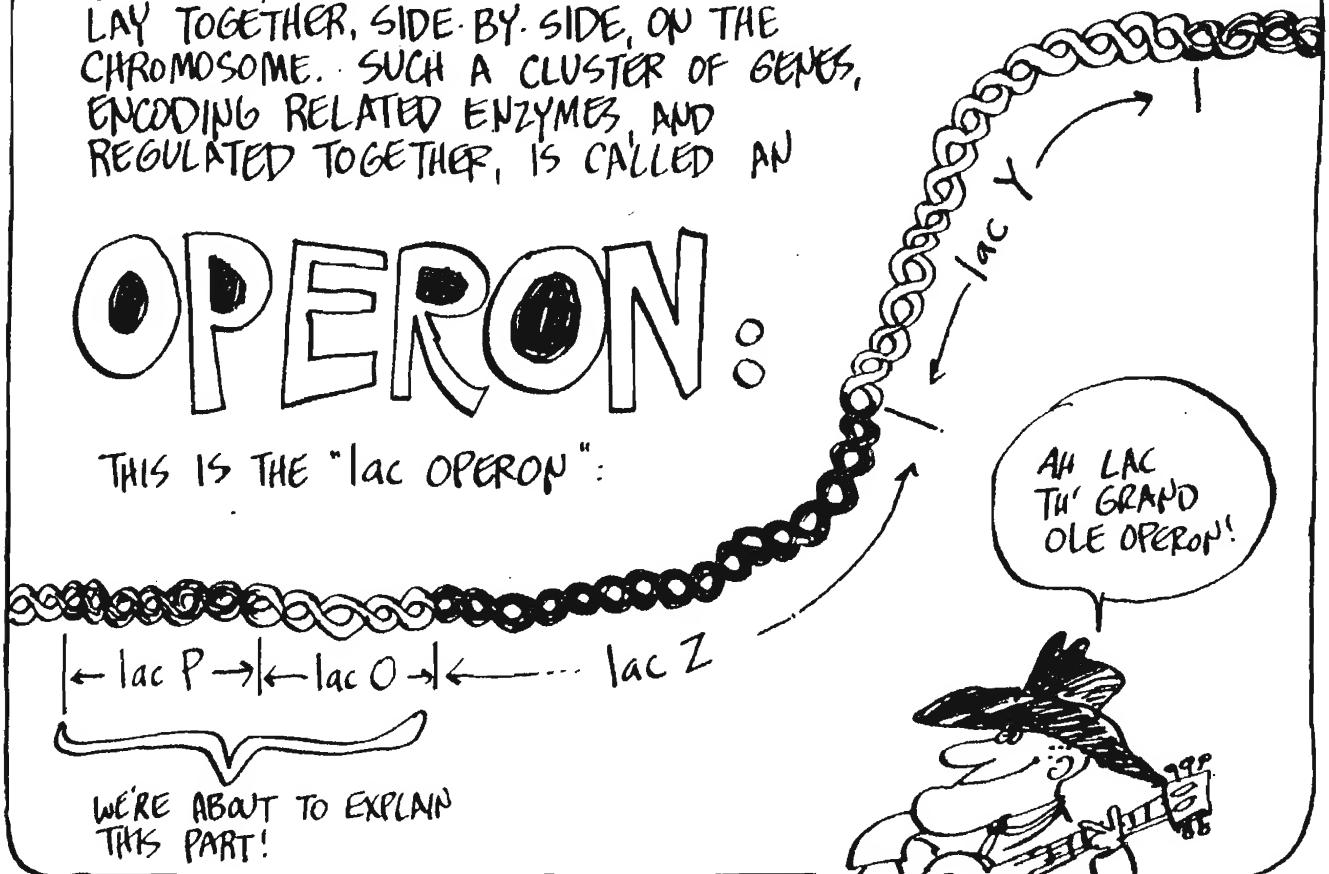


THIS EXPERIMENT WAS MORE DIFFICULT THAN A CHEESE SOUFFLÉ!

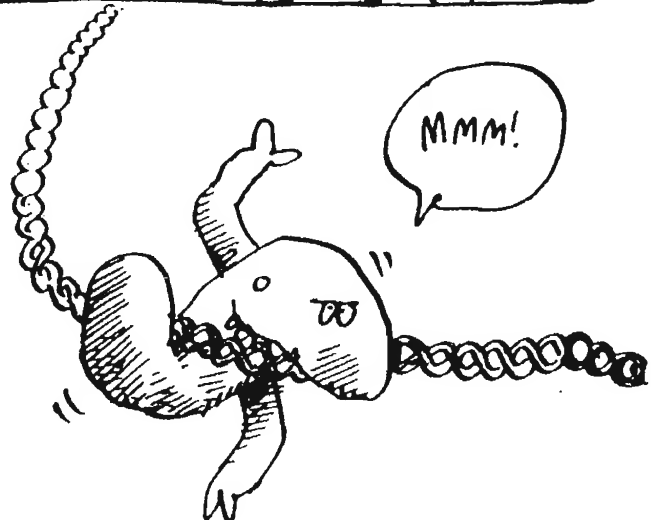
FIRST, THEY FOUND THAT THE GENES FOR Y AND Z, CALLED "lac Y" AND "lac Z," LAY TOGETHER, SIDE-BY-SIDE, ON THE CHROMOSOME. SUCH A CLUSTER OF GENES, ENCODING RELATED ENZYMES, AND REGULATED TOGETHER, IS CALLED AN

OPERON:

THIS IS THE "lac OPERON":



AT THE START OF THIS (AND EVERY) OPERON IS A **PROMOTER** REGION, HERE CALLED lac P. THIS IS THE SITE WHERE THE ENZYME **RNA POLYMERASE** BINDS ONTO THE DNA TO BEGIN TRANSCRIBING THE MESSAGE INTO mRNA. (SEE p. 133.)

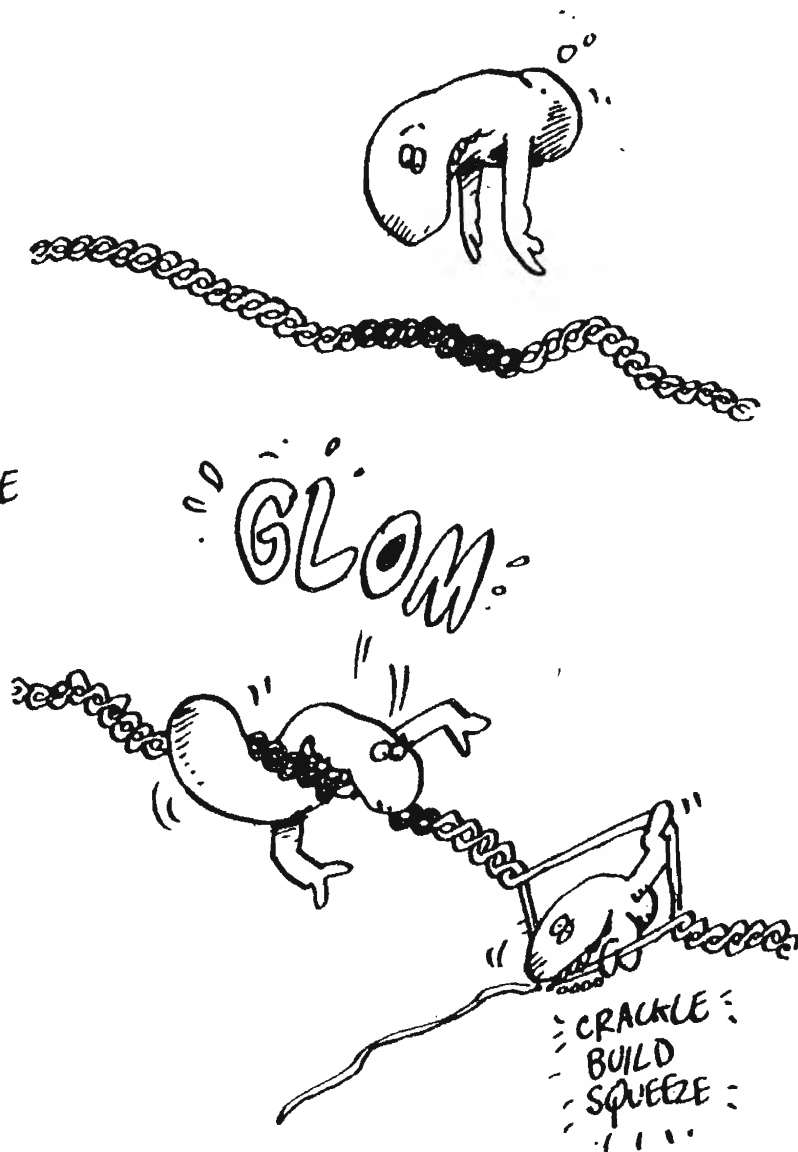


The First

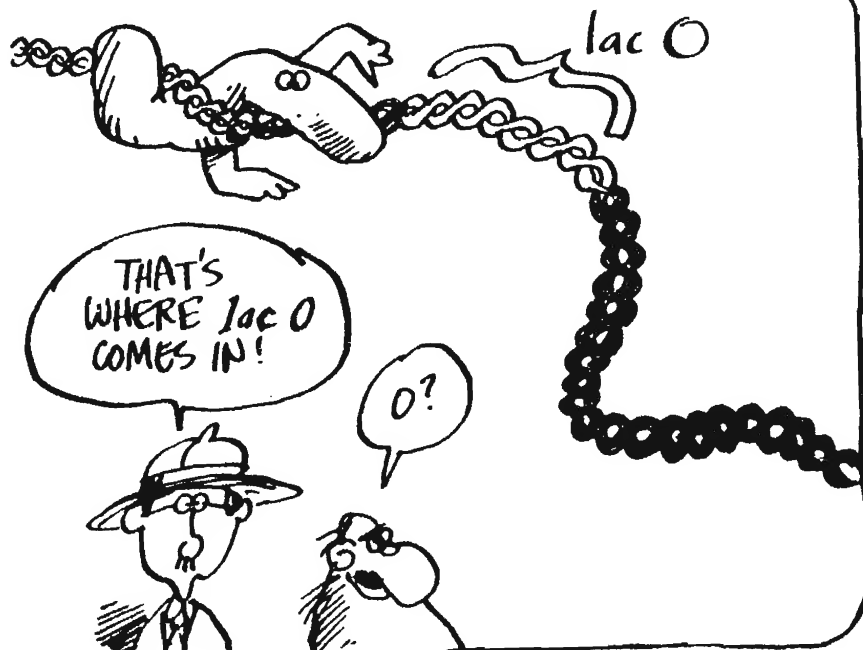
TYPE OF REGULATION IS SIMPLE:
SOME PROMOTER REGIONS ARE MORE ATTRACTIVE TO RNA POLYMERASE THAN OTHERS.



THE GENE FOR A MUCH-USED ENZYME HAS A PROMOTER WHERE POLYMERASE MAY EASILY BEGIN TRANSCRIPTION, WHILE A GENE ENCODING AN ENZYME NEEDED IN SMALL AMOUNTS WILL HAVE A MORE "DIFFICULT" PROMOTER REGION.



WHAT ABOUT THE LACTOSE OPERON, WHOSE ENZYMES ARE SOMETIMES NEEDED IN QUANTITY (WHEN LACTOSE IS PRESENT), BUT OTHERWISE NOT NEEDED AT ALL ??



MONOD + JACOB'S IDEA:
THERE IS A PROTEIN,

THE REPRESSOR,

WHICH SITS ON THE DNA
AT A SPOT BETWEEN
THE PROMOTER AND
THE FIRST GENE, *lacZ*.
THIS SPOT IS CALLED
THE **OPERATOR**,
lacO.



THE REPRESSOR —
WHICH THE FRENCH
SCIENTISTS NEVER
OBSERVED DIRECTLY —
SIMPLY BLOCKS THE
ACTION OF RNA POLYMERASE
AND SO SHUTS DOWN
THE ENTIRE OPERON.

ONE MORE THING ABOUT THE REPRESSOR: IT CAN ALSO BIND
TO **LACTOSE*** — BUT DOING SO CAUSES THE REPRESSOR TO
"FLEX" AND RELEASE THE DNA:



* ACTUALLY NOT LACTOSE ITSELF, BUT A DERIVATIVE SUBSTANCE — BUT NEVER MIND !!

IN THE NORMAL STATE OF AFFAIRS, THE REPRESSOR SITS ON THE OPERATOR, REPRESSING THE GENE:



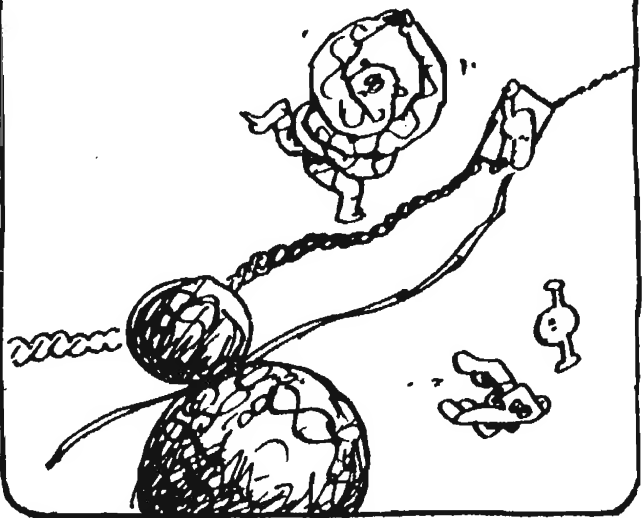
ALONG COMES A LITTLE LACTOSE, ATTRACTING THE REPRESSOR:



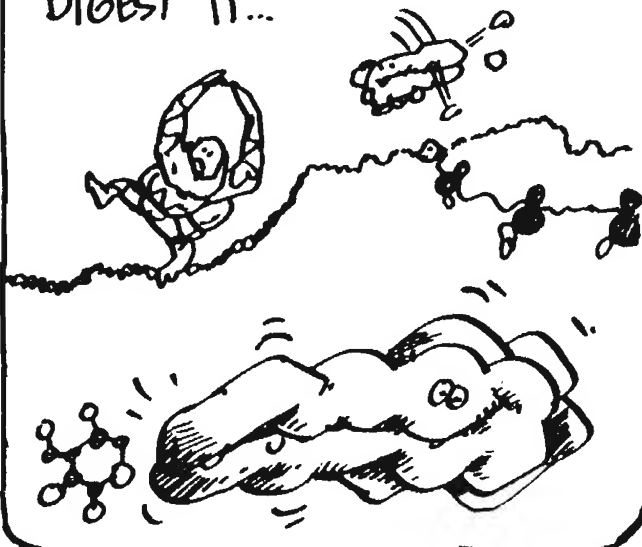
IT FLEXES, GRASPING THE SUGAR, AND RNA POLYMERASE SLIPS THROUGH!!



THE ENTIRE OPERON IS THEN EXPRESSED REPEATEDLY.



THE NEWLY MADE PROTEINS BRING IN MORE LACTOSE AND DIGEST IT...



FINALLY, WHEN ALL THE LACTOSE IS GONE, THE REPRESSOR UNFLEXES AND RETURNS TO ITS SPOT ON THE CHROMOSOME.



REPRESSORS
TURN OUT TO BE
A COMMON WAY
TO REGULATE
"INDUCIBLE" ENZYMES—
I.E., ENZYMES WHICH
ARE MADE IN
RESPONSE TO A
CHEMICAL-LIKE
LACTOSE...
BUT DESPITE THIS
BRILLIANT IDEA,
MONOD AND JACOB
COULD NEVER
ACTUALLY FIND A
REPRESSOR. IT
REMAINED A
THEORETICAL POSSIBILITY...

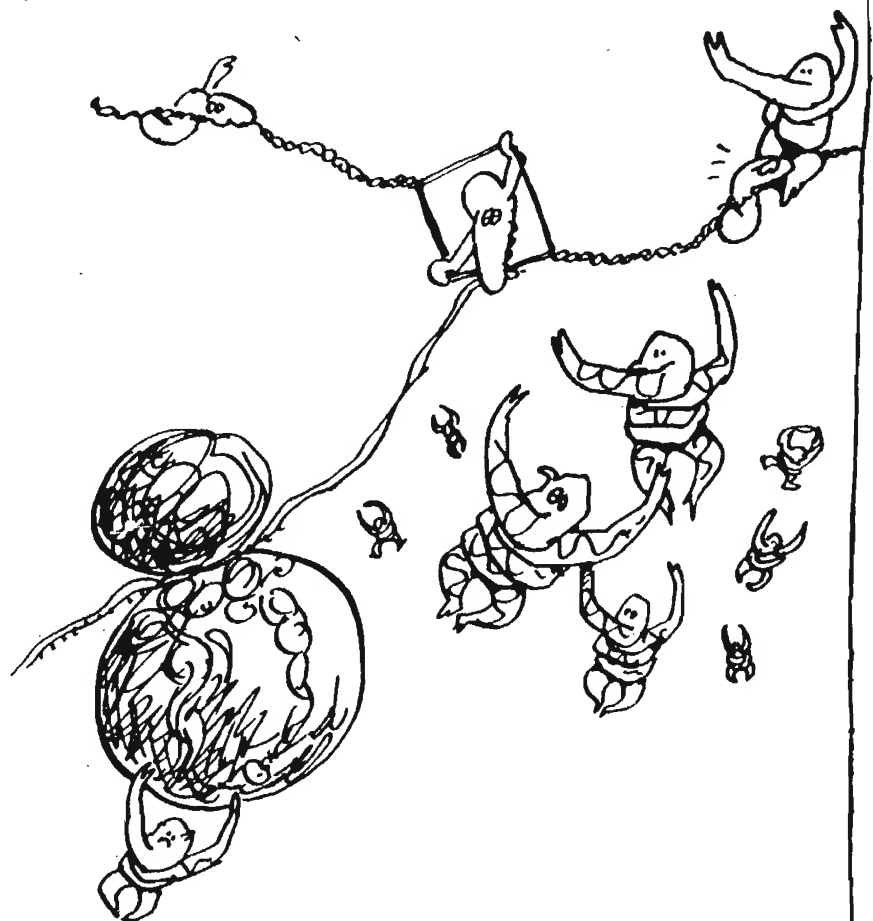


THESE
REPRESSORS ARE
MORE ELUSIVE THAN
A PERFECT
SAUCE BÉARNAISE...



...UNTIL 1967, WHEN WALTER GILBERT AND B. MÜLLER-HILL, USING
VERY REFINED TECHNIQUES, WERE ABLE TO ISOLATE THE ELUSIVE
PROTEINS.

THEIR RESULTS MADE
PLAIN WHY IT
HAD BEEN SO HARD
TO FIND THEM:
A SINGLE *E. COLI*
BACTERIUM HAS
ONLY FIVE TO
TEN MOLECULES
OF LAC REPRESSOR.
LATER, GILBERT
MANAGED TO
BREED MUTANT
E. COLI THAT
PRODUCED IT
IN MUCH LARGER
AMOUNTS....



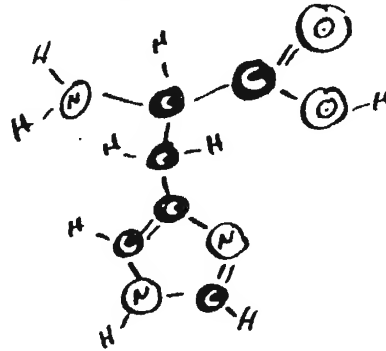
ANOTHER METHOD OF GENE
REGULATION GOES BY THE NAME OF:

ATTENUATION

AND ITS
SUCCESSOR,
ELEVEN-TUATION!

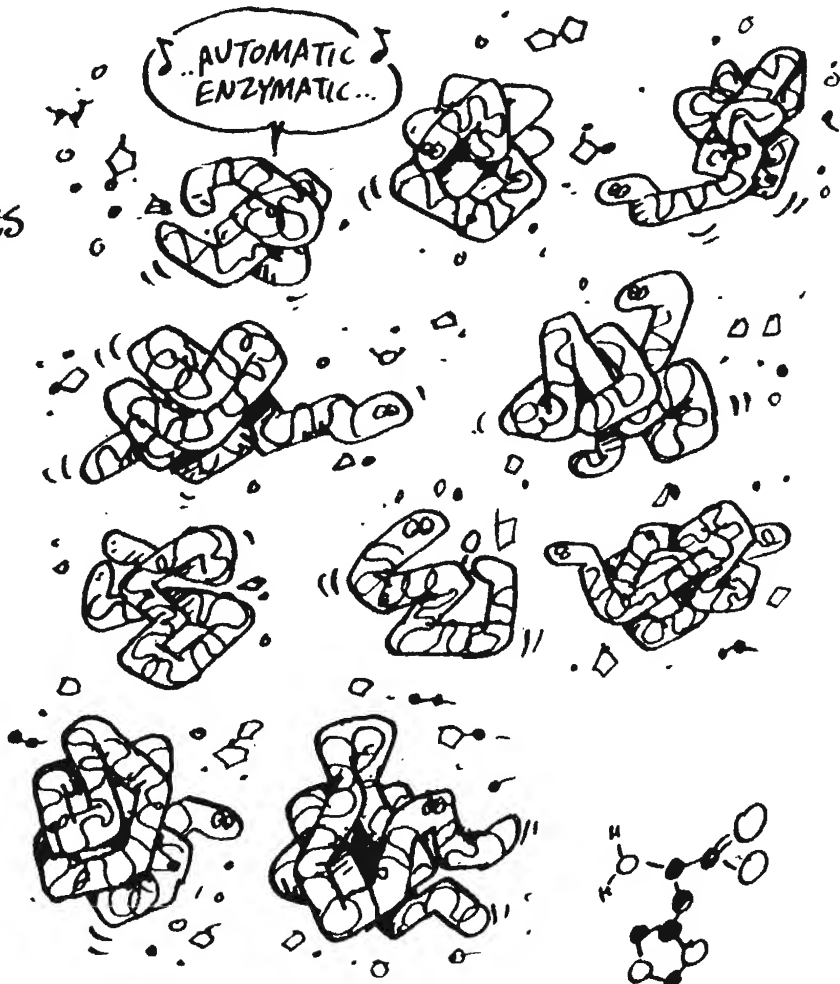


THIS GOVERNS AN E. COLI
OPERON RESPONSIBLE FOR
CONSTRUCTING THE AMINO
ACID HISTIDINE.

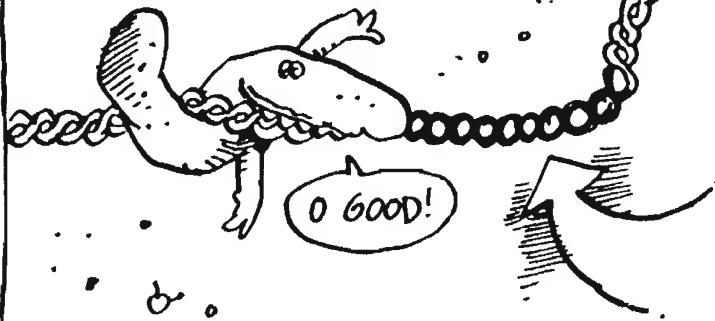


WHEN E. COLI
RUNS LOW ON
THIS ESSENTIAL
STUFF, THE
BACTERIUM PRODUCES
A GROUP OF
NINE PROTEINS,
WHICH CAN
BUILD HISTIDINE
MOLECULES
FROM SCRATCH.

AN
ENZYMATIC
ASSEMBLY
LINE!

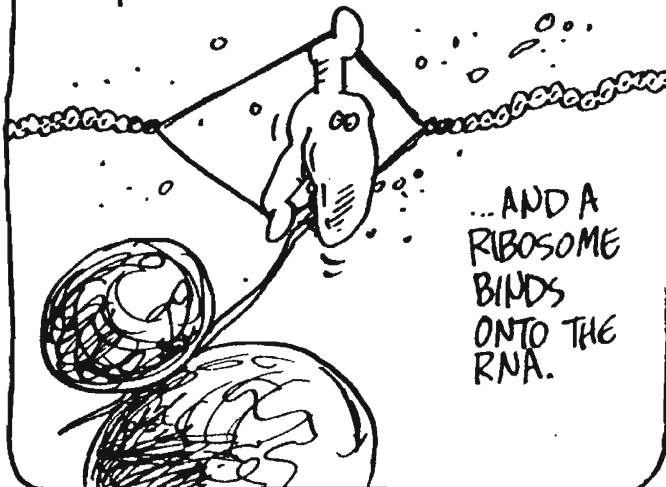


AS BEFORE, ALL 9 ENZYMES HAVE THEIR GENES CLUSTERED INTO AN OPERON, WITH AN INITIAL PROMOTER REGION. UNLIKE THE LAC OPERON, THIS ONE HAS NO PLACE FOR A REPRESSOR.



INSTEAD, THERE IS A "LEADER SEQUENCE" ENCODING A PEPTIDE RICH IN HISTIDINE—THE VERY STUFF WE'RE TRYING TO MANUFACTURE.

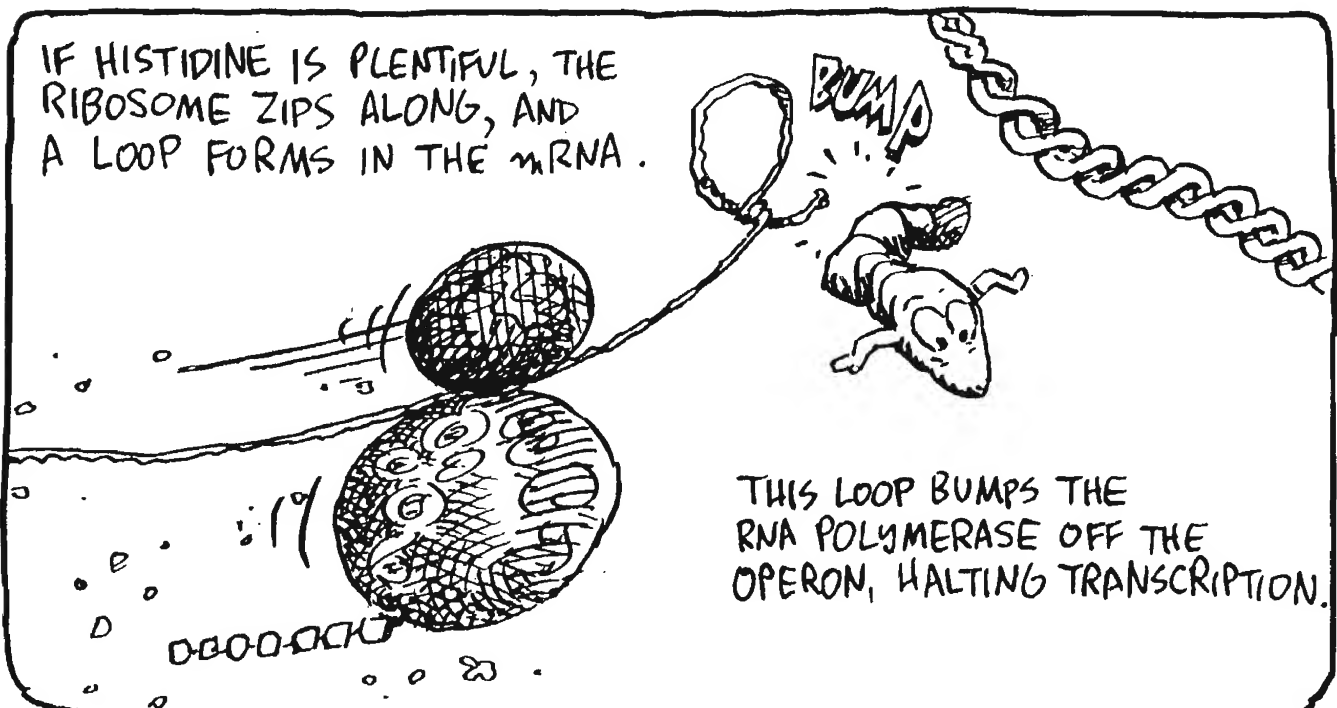
RNA POLYMERASE BEGINS BY TRANSCRIBING THE LEADER SEQUENCE...



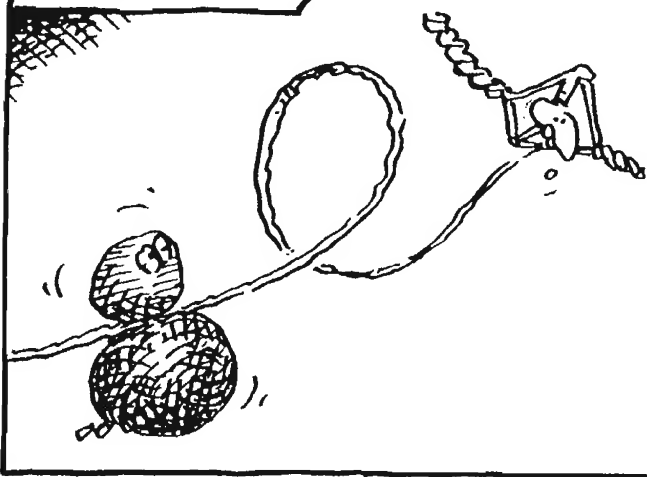
THE LEADER SEQUENCE ENCODES 7 HISTIDINES IN A ROW



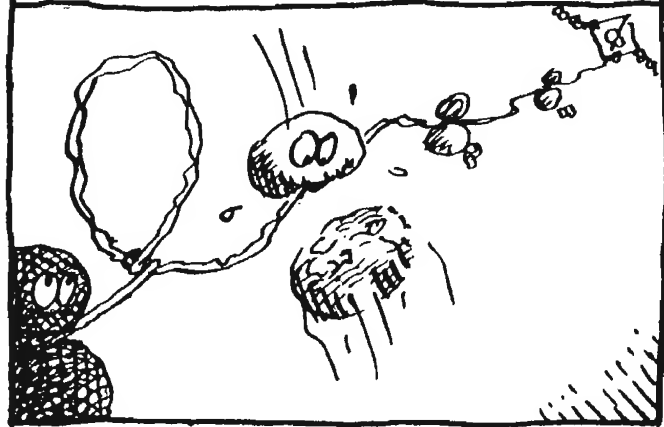
IF HISTIDINE IS PLENTIFUL, THE RIBOSOME ZIPS ALONG, AND A LOOP FORMS IN THE mRNA.



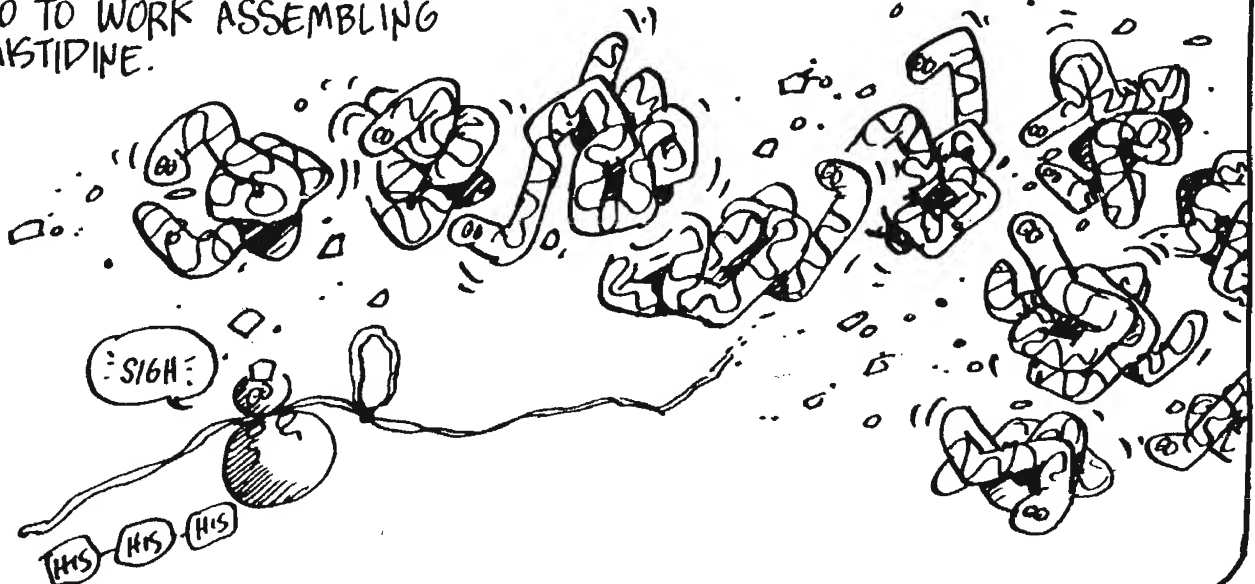
IF, ON THE OTHER HAND, HISTIDINE IS IN SHORT SUPPLY, THE RIBOSOME FALLS BEHIND THE POLYMERASE.



IN THIS CASE, A **DIFFERENT** LOOP FORMS, WHICH, BY PREVENTING THE FIRST LOOP, ENABLES THE POLYMERASE TO GO ON, AND THE OPERON IS EXPRESSED!



THE NEWLY MADE PROTEINS GO TO WORK ASSEMBLING HISTIDINE.



RESULT?

A SHORTAGE OF HISTIDINE TURNS THE GENE **ON**, WHILE A HISTIDINE GLUT TURNS IT **OFF**.

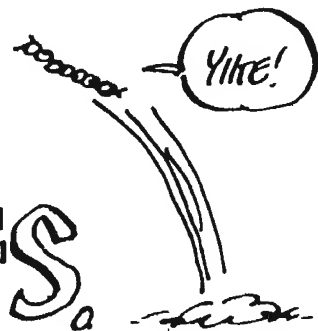




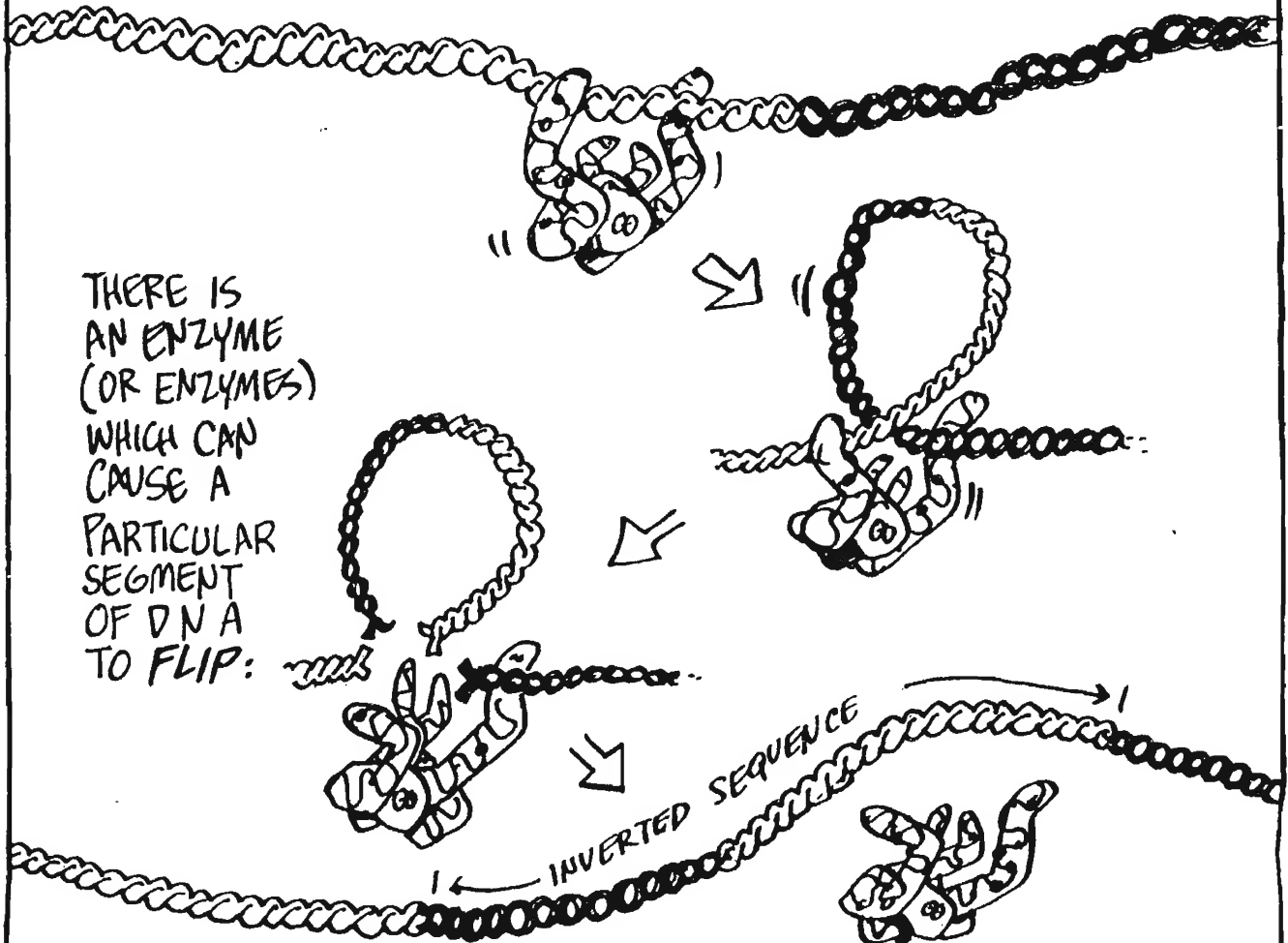
THE PORTRAIT OF THE GENE, AS SKETCHED BY MENDEL, AND FILLED IN BY LATER GENERATIONS, DEPICTED AN OBJECT FIXED AND UNCHANGING, ASIDE FROM OCCASIONAL MUTATIONS.

MORE RECENT DISCOVERIES SHOW A GENE MORE MOVABLE AND PLASTIC... IN FACT, AN IMPORTANT MEANS OF GENE REGULATION DEPENDS ON WHAT WE MIGHT CALL...

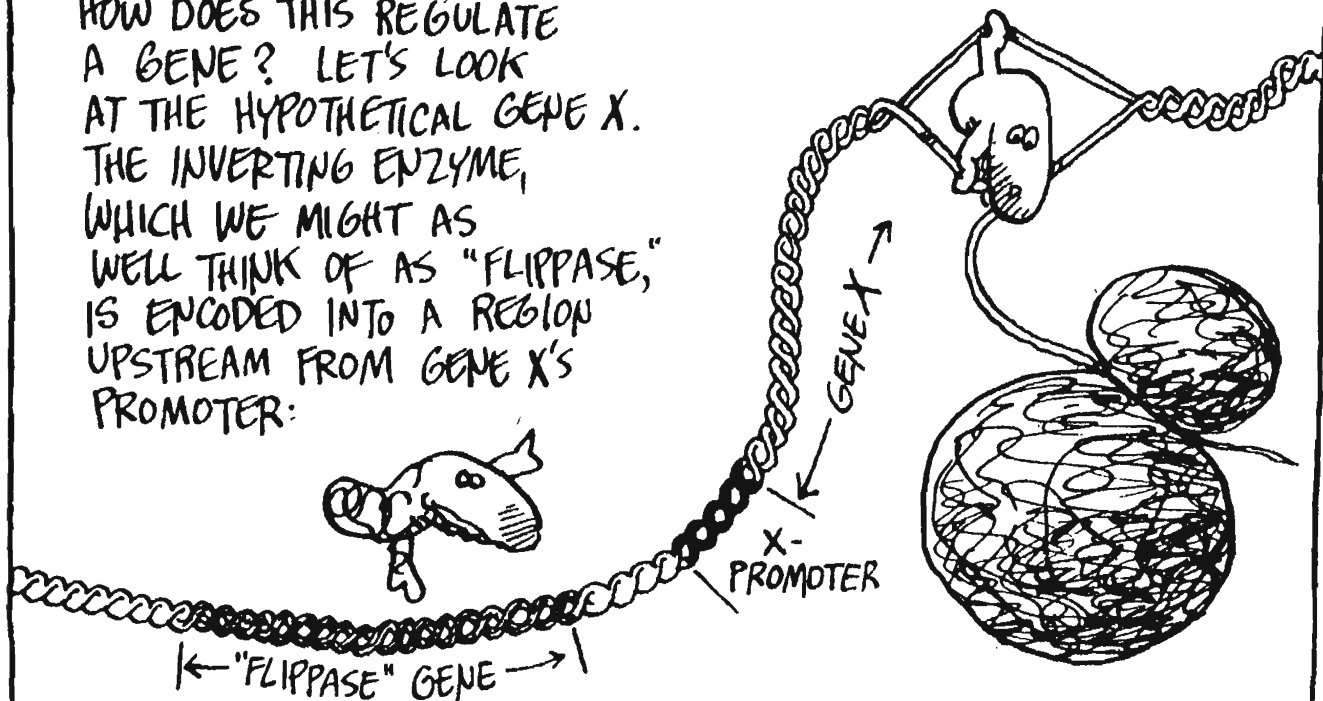
JUMPING GENES.



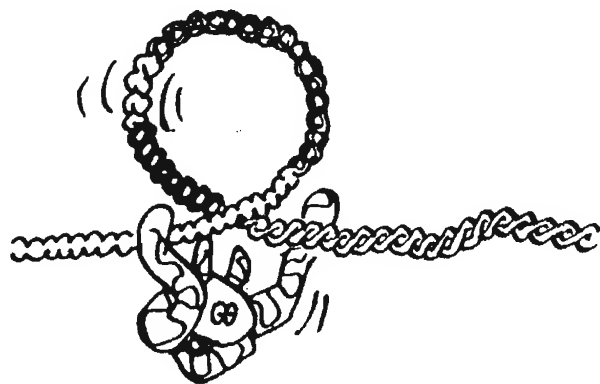
THERE IS AN ENZYME (OR ENZYMES) WHICH CAN CAUSE A PARTICULAR SEGMENT OF DNA TO FLIP:



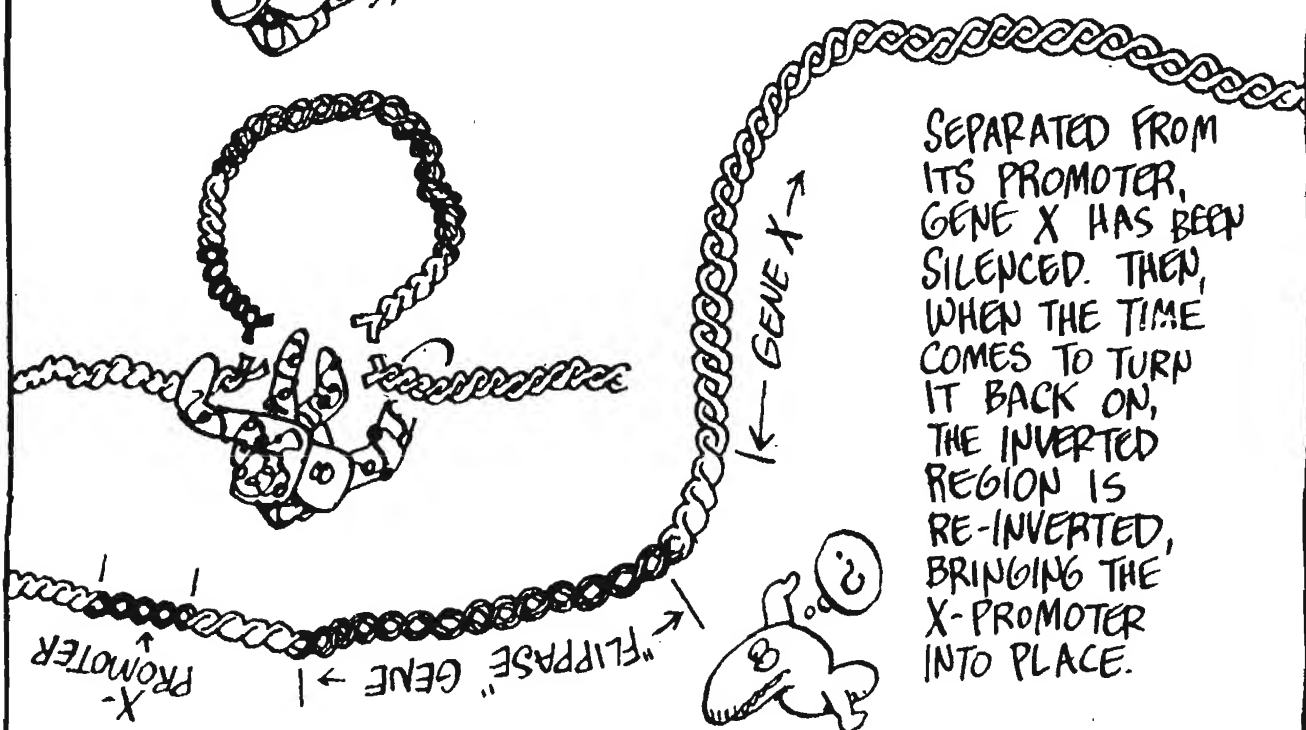
HOW DOES THIS REGULATE A GENE? LET'S LOOK AT THE HYPOTHETICAL GENE X. THE INVERTING ENZYME, WHICH WE MIGHT AS WELL THINK OF AS "FLIPPASE," IS ENCODED INTO A REGION UPSTREAM FROM GENE X'S PROMOTER:



SOMEHOW, WHEN IT'S TIME TO SHUT OFF GENE X, THE FLIPPASE GENE IS ACTIVATED, MAKING THE ENZYME.



IT INVERTS A SEGMENT INCLUDING ITS OWN GENE AND GENE X'S PROMOTER.



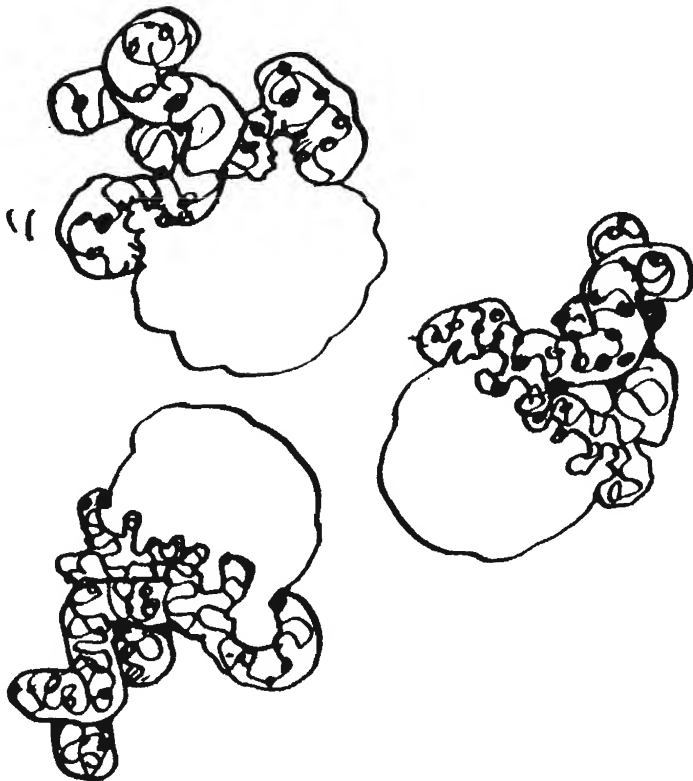
SEPARATED FROM ITS PROMOTER, GENE X HAS BEEN SILENCED. THEN, WHEN THE TIME COMES TO TURN IT BACK ON, THE INVERTED REGION IS RE-INVERTED, BRINGING THE X-PROMOTER INTO PLACE.

SUCH MOVABLE
SECTIONS, OR
TRANSPOSONS,

ARE COMMON IN BOTH
PROCARYOTES AND
EUCARYOTES. BESIDES
INVERTING, THEY CAN
JUMP FROM PLACE
TO PLACE, FROM
CHROMOSOME TO
CHROMOSOME. THE
FULL FUNCTION OF
TRANSPOSONS IS
STILL A MYSTERY.



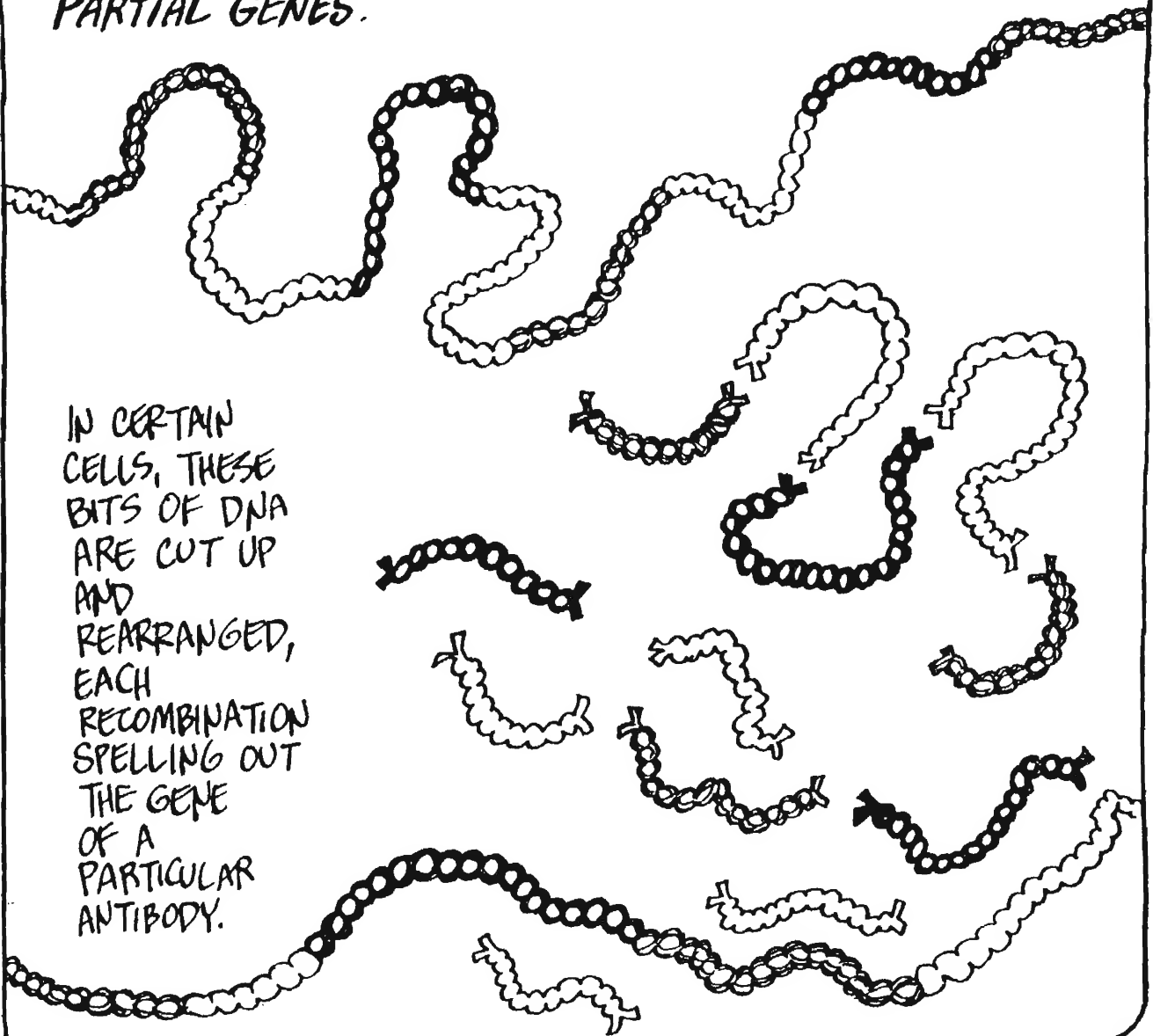
THE MOST SPECTACULAR EXAMPLES OF JUMPING GENES ARE
THE ONES ENCODING ANTIBODIES.



ANTIBODIES ARE
PROTEINS WHICH
SERVE AS THE BODY'S
DEFENSIVE WEAPONS.
THEY ATTACK
BACTERIA, VIRUSES,
AND OTHER
HARMFUL INVADERS.
THERE ARE LITERALLY
BILLIONS OF
POTENTIAL ANTIBODIES,
EACH KEYED TO
THE EXACT SHAPE
OF ITS "ENEMY."
HOW CAN SO MANY
BE ENCODED IN
GENES?

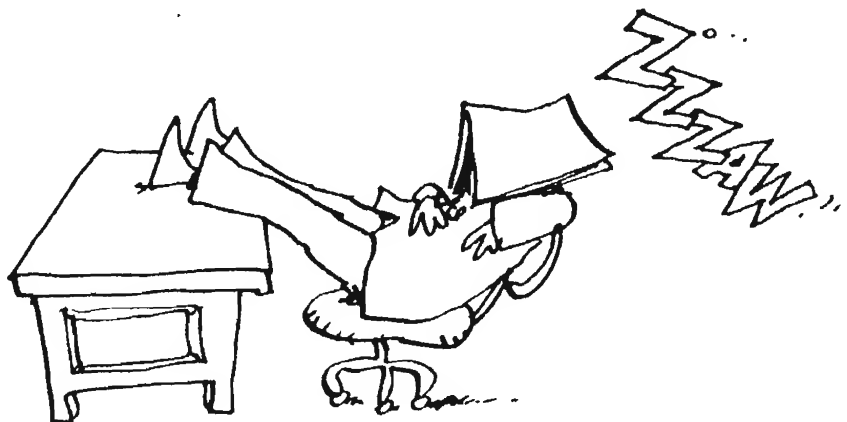
RATHER THAN HAVING BILLIONS OF GENES FOR ANTIBODIES,
THE CHROMOSOMES CARRY A "TOOL KIT" OF A FEW HUNDRED
PARTIAL GENES.

IN CERTAIN
CELLS, THESE
BITS OF DNA
ARE CUT UP
AND
REARRANGED,
EACH
RECOMBINATION
SPELLING OUT
THE GENE
OF A
PARTICULAR
ANTIBODY.



HOW THE ORGANISM REGULATES THIS PROCESS IS STILL A RIDDLE,
AS ARE MOST MATTERS OF EUKARYOTIC GENE REGULATION: THE
QUESTION OF HEMOGLOBIN (P. 163), FOR EXAMPLE, REMAINS
WITHOUT AN ANSWER.

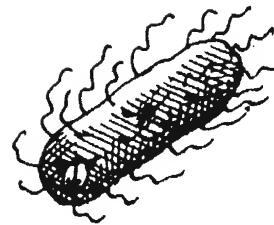
IT'S CLEAR THAT
THE FLEXIBLE GENES
OF EUKARYOTES
WILL BE AN ACTIVE
AREA OF RESEARCH
IN YEARS TO
COME.



GENETIC ENGINEERING

LIVING CELLS ARE
NOT THE ONLY ONES
CAPABLE OF REARRANGING
GENES!! NOW SCIENTISTS
TOO HAVE THE POWER...

...A GREATER POWER
THAN BIOLOGISTS
HAVE EVER KNOWN...



FOR ONE THING, PEOPLE
CAN NOW **SPLICE**
TWO PIECES OF DNA
IN THE TEST TUBE —
JUST LIKE SPLICING
FILM...



HMM...
I'LL ATTACH "GOD'S
LITTLE ACRE" TO
"VIVA VILLA!"...

I'LL CALL IT
"GODZILLA!"

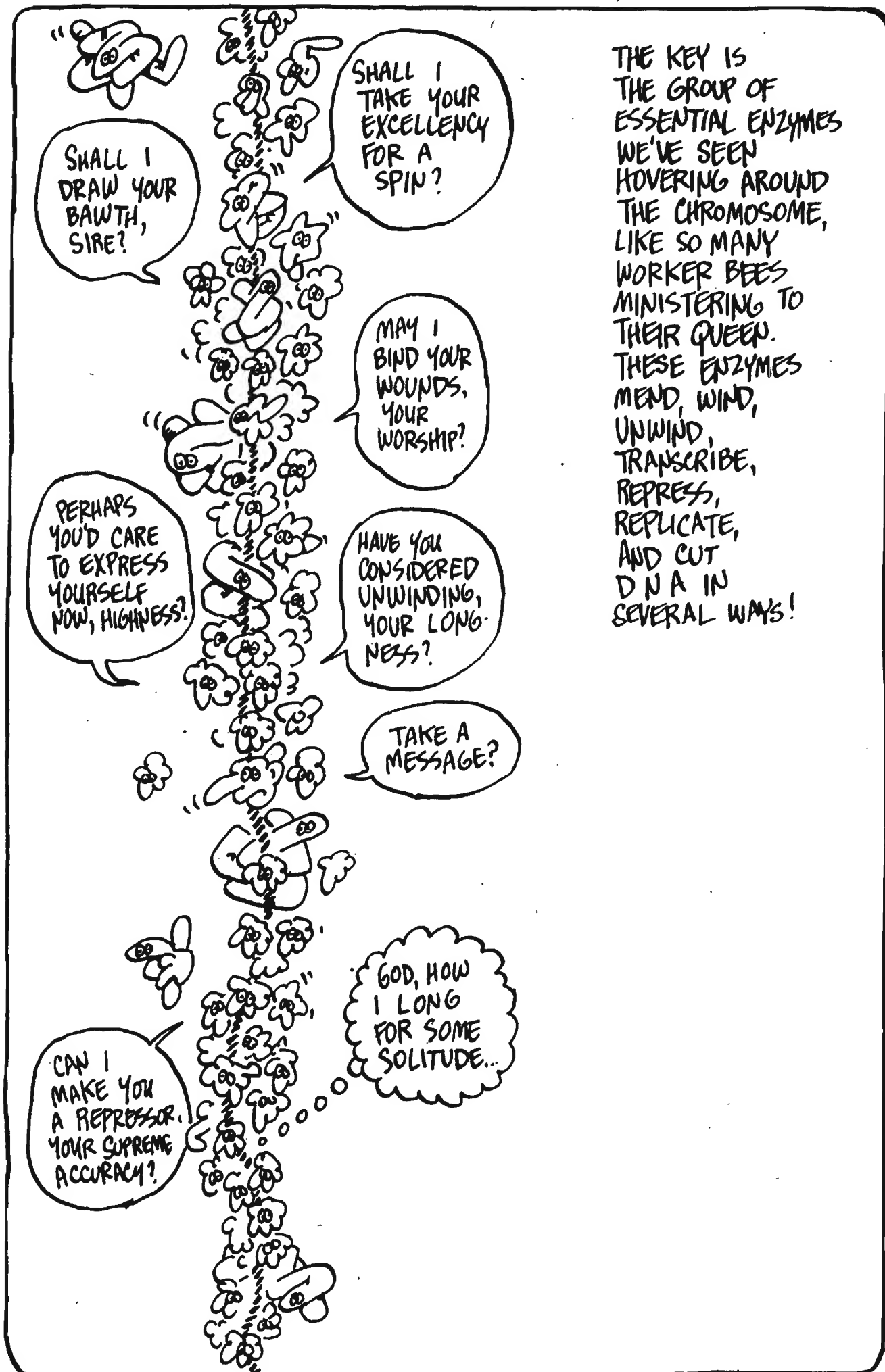
THE COMBINATIONS CAN BE PRETTY BIZARRE: MOST COMMONLY,
HUMAN GENES ARE ATTACHED TO THOSE OF A BACTERIUM,
LIKE *E. COLI*...

WHAT ARE YOU —
A MAN OR A
MICROBE?



THIS IS WHAT
YOU CALL

**RECOMBINANT
DNA**



GENE SPLICING DEPENDS ON A SPECIAL TYPE OF CUTTING ENZYME CALLED A RESTRICTION ENDONUCLEASE, OR RESTRICTION ENZYME FOR SHORT.

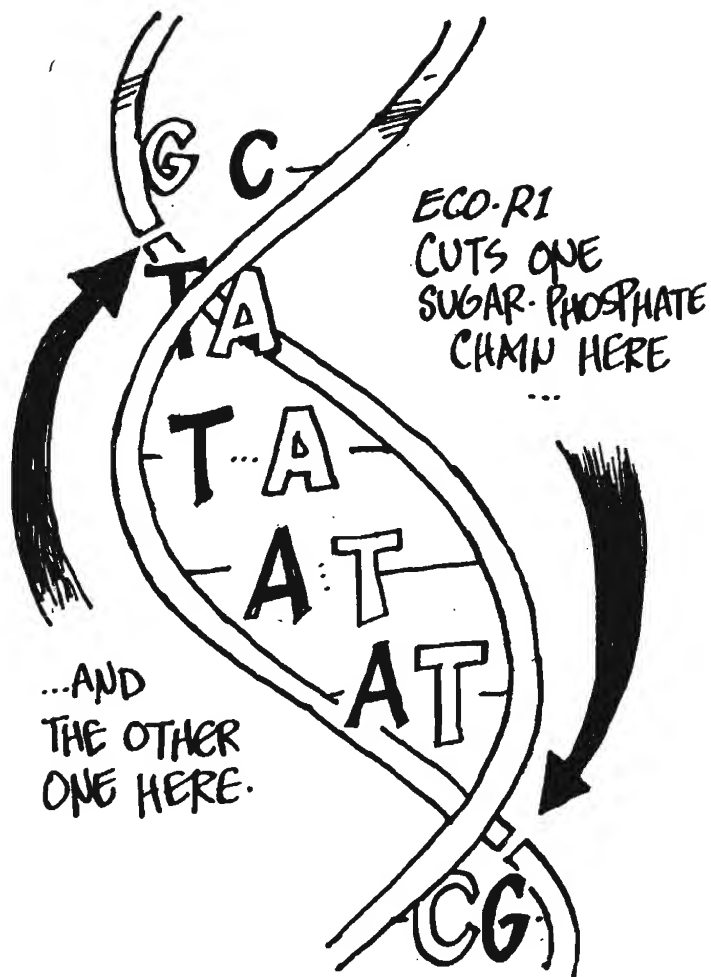
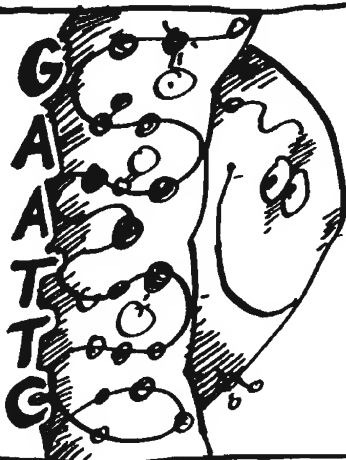


A RESTRICTION ENZYME MAKES A "STAGGERED NICK" IN DNA AT A SPECIFIC SEQUENCE OF BASES.



THE ENZYME *ECO*.R1, FOR EXAMPLE, RECOGNIZES ONLY THE SEQUENCE

-G-A-A-T-T-C-
-C-T-T-A-A-G-



THIS CREATES TWO PIECES OF DNA WITH IDENTICAL T-T-A-A "TAILS." (BECAUSE C-T-T-A-A-G IS THE SAME AS ITS COMPLEMENT READ BACKWARDS!)



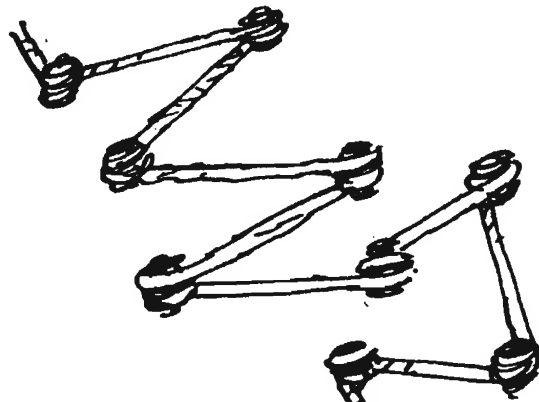
E. COLI USES
ECO-R1 TO
CHOP UP
"ENEMY" VIRAL
DNA,
BUT HUMANS
HAVE PUT
IT TO
CONSTRUCTIVE
USE.

YOU'RE
BEATING
MY SWORDS
INTO
PLOWSHARES?

NO... STOCK SHARES
IN GENETIC ENGINEERING
COMPANIES..



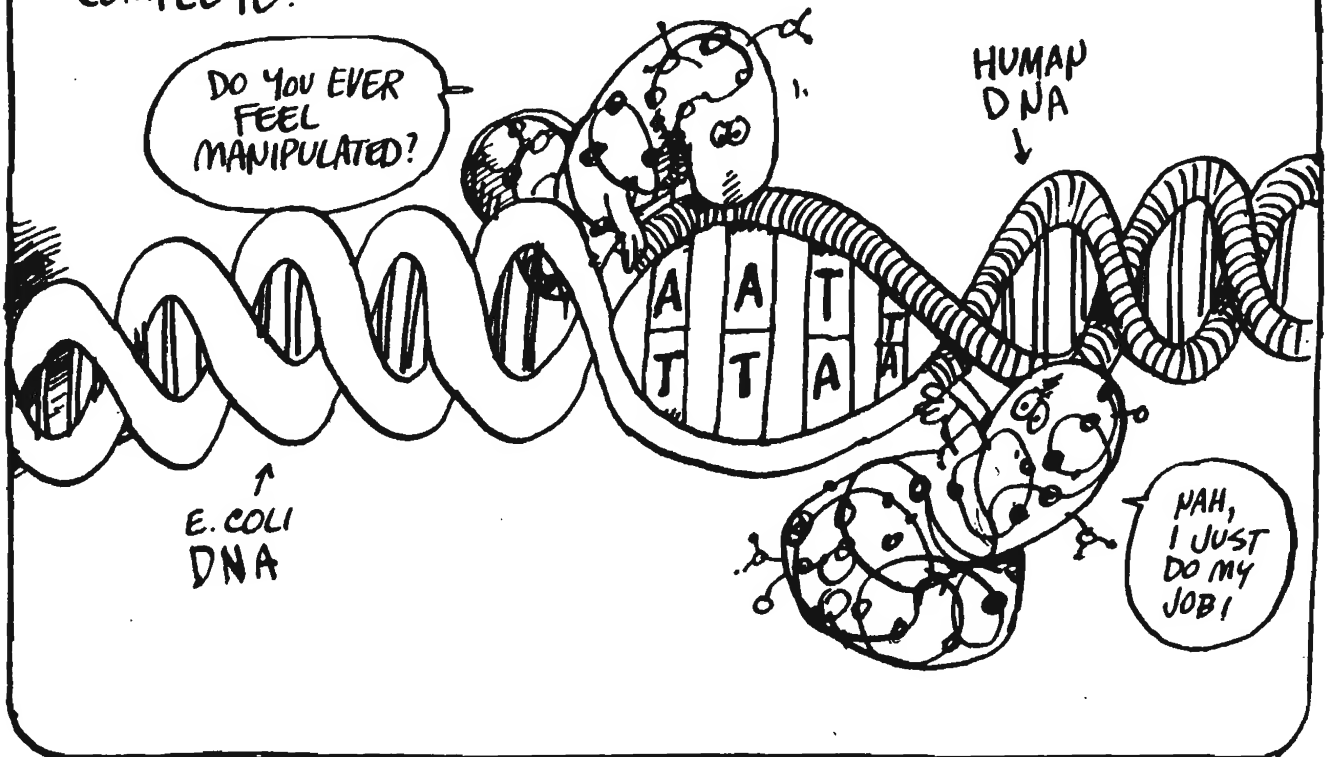
THEY BEGIN WITH DNA FROM TWO DIFFERENT SOURCES, SAY
E. COLI AND HUMAN, AND TREAT BOTH WITH ECO-R1 IN THE
SAME TEST TUBE.



THIS GIVES THEM BOTH
THE "SELF-BACKWARDS-
COMPLEMENTARY" TAIL,
T-T-A-A.



THE TAILS SNAP TOGETHER, AND, AFTER TREATMENT WITH **LIGASE**, AN ENZYME THAT SEALS NICKS IN THE SUGAR-PHOSPHATE CHAIN, THE **RECOMBINANT DNA** IS COMPLETE!



WHAT CAN YOU DO WITH THIS HYBRID MOLECULE? WHAT HAPPENS WHEN RECOMBINANT DNA IS INSERTED INTO A LIVING SYSTEM? UNDER SOME CONDITIONS, IT TURNS OUT THAT GENE SPLICING CAN BE USEFUL IN PRACTICE...



THE TECHNIQUE IS CALLED

GENE CLONING

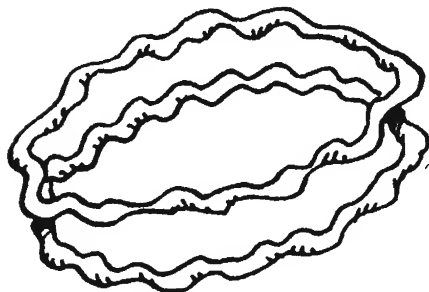
AND IT WORKS LIKE THIS:

FIRST, CHOOSE A HUMAN GENE ENCODING SOME USEFUL PROTEIN.

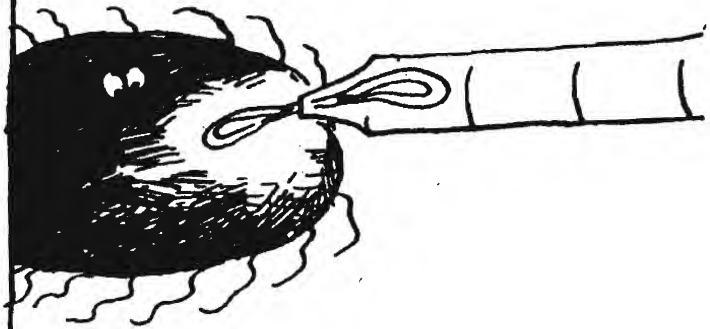


IS THERE A PROTEIN THAT PUTS YOU THROUGH MEDICAL SCHOOL?

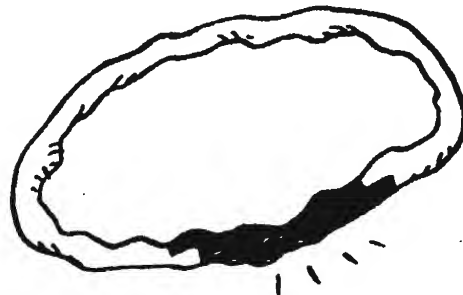
FOR YOUR BACTERIAL DNA, YOU NEED SOMETHING THAT WILL BE REPLICATED ONCE IT'S RETURNED TO THE CELL — A "VECTOR," SO-CALLED.



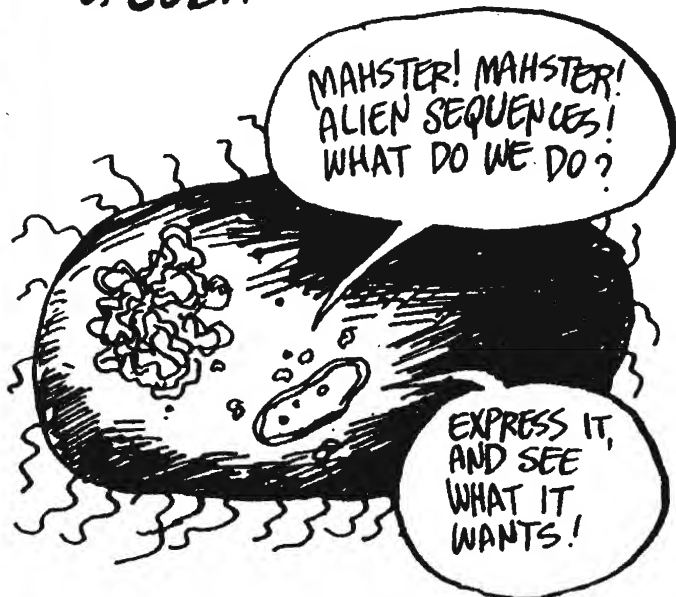
LUCKILY, *E. COLI* HAS SMALL RINGS OF DNA CALLED **PLASMIDS**, SEPARATE FROM THE CHROMOSOME. YOU CHOOSE (OR ENGINEER!) A PLASMID CONTAINING THE SEQUENCE G·A·A·T·T·C, AND REMOVE IT FROM THE BACTERIUM.



JUST AS ABOVE, YOU **SPLICE** THE HUMAN GENE INTO THE PLASMID —



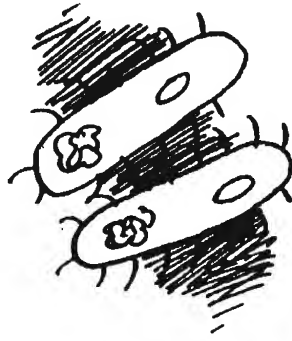
AND PUT IT BACK INTO *E. COLI*.



BE FRUITFUL
AND DIVIDE!

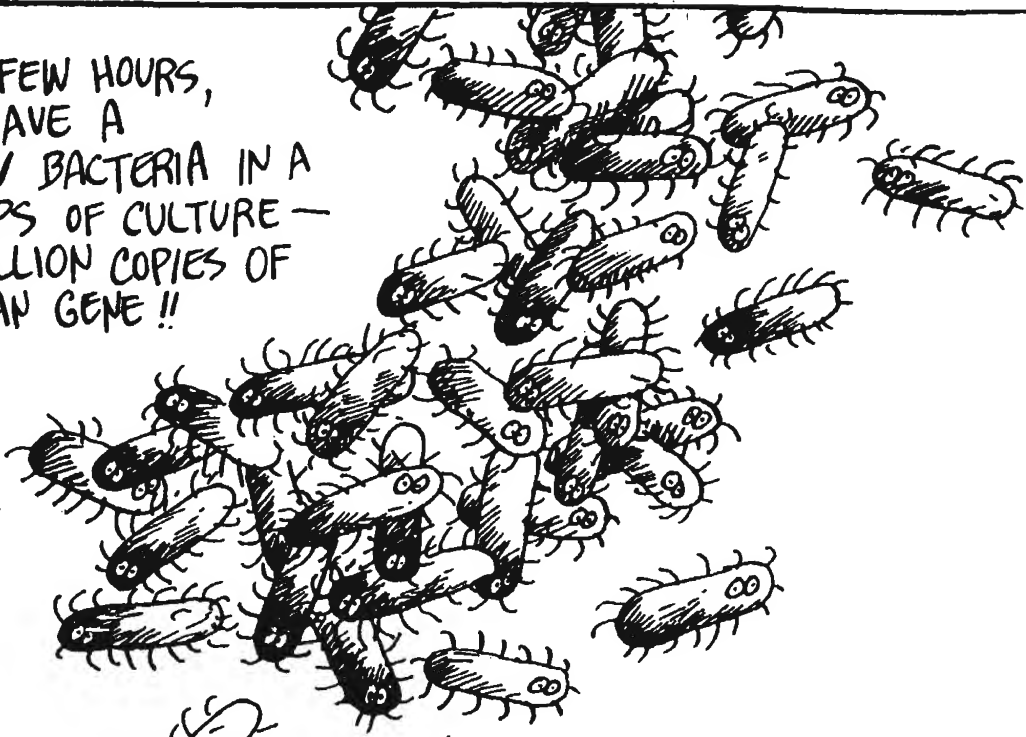


NOW YOU
FEED THE
BACTERIUM
AND LET
IT BREED.



THE PLASMID
IS REPLICATED
ALONG WITH
EVERYTHING
ELSE IN
THE BACTERIUM.

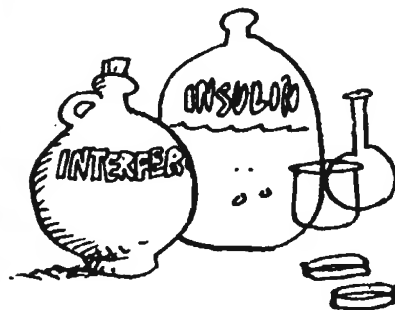
WITHIN A FEW HOURS,
WE CAN HAVE A
BILLION BACTERIA IN A
FEW DROPS OF CULTURE —
AND A BILLION COPIES OF
THE HUMAN GENE !!



IF WE'VE
INCLUDED THE
PROPER REGULATORY
REGIONS AS WELL,
THE BACTERIA
SHOULD EXPRESS
THE GENE, AND
WE CAN EXTRACT
SUBSTANTIAL
AMOUNTS OF
THE HUMAN
PROTEIN.
MIRACULOUS!



PRAISE
BE!



THE PROCEDURE SOUNDS SIMPLE — AND, IN PRINCIPLE, IT IS. IN PRACTICE IT CAN BE MOST COMPLICATED, BUT THE FOLKS IN THE LABS HAVE SOLVED MOST OF THOSE PRACTICAL PROBLEMS. WE CAN NOW CLONE JUST ABOUT ANY GENE WE WANT... USUALLY IN *E. COLI*, BUT OTHER FAST-GROWING ORGANISMS WORK, AS WELL, EVEN EUKARYOTES LIKE YEAST —

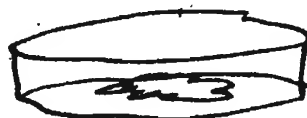


HI! NOT ONLY DO I FULFILL THE MINIMUM DAILY REQUIREMENT OF VITAMINS A, B, C, D, AND K, BUT ALSO I TASTE LIKE ROAST DUCKLING AND PREVENT CANCER!

'BREAD OF THE FUTURE!'

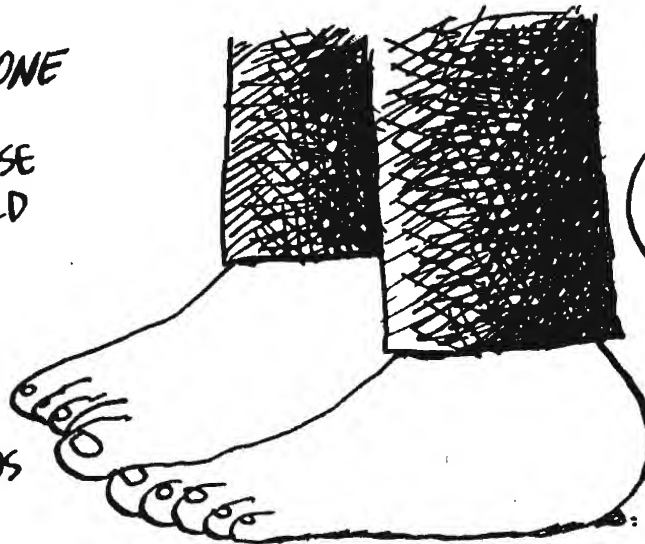
IT'S EVEN POSSIBLE TO CLONE GENES INTO HUMAN CELLS, BUT SO FAR IT ONLY WORKS IN A DISH, NOT IN A REAL PERSON...

BUT ONE OF THESE DAYS...



AT LEAST 3 PROTEINS NOW PRODUCED BY RECOMBINANT DNA HAVE MEDICAL POSSIBILITIES...

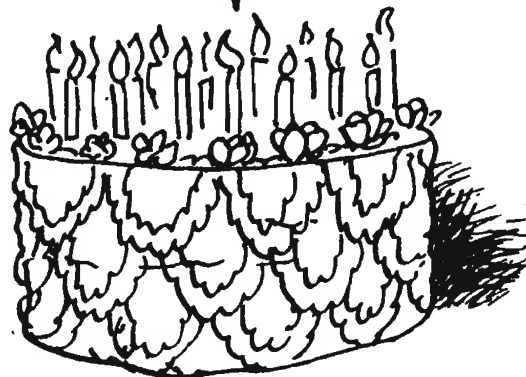
HUMAN GROWTH HORMONE PREVENTS ONE TYPE OF DWARFISM. PEOPLE WHOSE GENETIC MAKE-UP WOULD OTHERWISE LEAVE THEM A BIT "SHORT," CAN GROW NORMALLY IF GIVEN ADEQUATE DOSES. SO FAR, DEMAND STILL EXCEEDS SUPPLY, BUT NOT FOR "LONG"!



I THINK
I O.D.'D!

INSULIN, WHICH BREAKS DOWN SUGAR IN THE BLOOD, HAS LONG BEEN MADE BY OTHER MEANS... BUT SHOULD NOW BECOME MORE PLENTIFUL, AND POSSIBLY CHEAPER, MAKING LIFE EASIER FOR DIABETICS —

LET THEM EAT CAKE!



INTERFERON, THE VIRUS-FIGHTER, USED TO BE SO SCARCE IT COST A TRILLION DOLLARS AN OUNCE — BUT NOW IT'S MADE BY THE VASTFUL BY TRILLIONS OF *E. COLI*. UNFORTUNATELY, NO ONE KNOWS EXACTLY WHAT TO DO WITH IT, THOUGH CLINICAL TRIALS CONTINUE AMID HIGH HOPES...

IT MAY CURE CANCER
OR THE COMMON COLD!





SUDDENLY, GENE-SPLICING HAS BECOME **BIG BUSINESS!**

ZOOM-ZYME
A GROWTH INDUSTRY

LURED BY THE PROSPECT OF PROFITS FROM PROTEINS, VENTURE CAPITALISTS HAVE BEEN ENTICING BIOLOGY PROFESSORS INTO A NEW SORT OF ENTERPRISE: THE GENETIC ENGINEERING COMPANY.



YOU'RE OUR KIND OF FOLKS, PROF-

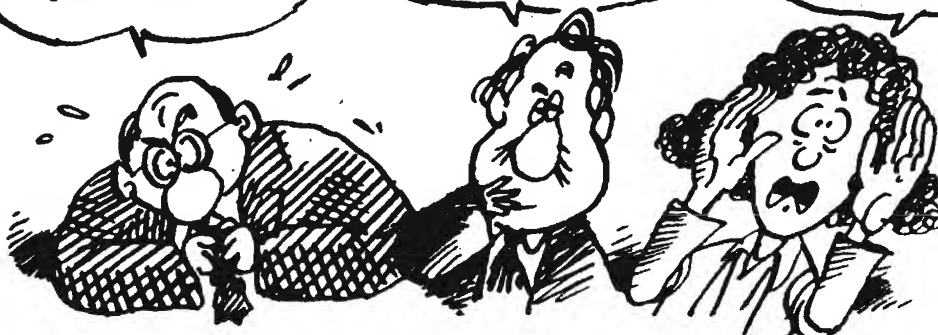
YOU MAKE HUMAN PROTEIN FROM TINY BACTERIA - WE MAKE FORTUNES FROM MICROSCOPIC INVESTMENTS...

BACK IN THE UNIVERSITY, THIS IS THE CAUSE OF SOME CONCERN...

IS FREE INQUIRY POSSIBLE IF OUR DISCOVERIES BECOME TRADE SECRETS?

CAN OPEN RESEARCH BE GUIDED BY THE PROFIT MOTIVE?

DO WE WANT TO DIRTY OUR HANDS WITH MERE MONEY?



... WHICH HASN'T SLOWED
THE GROWTH OF INDUSTRY
AT ALL!!

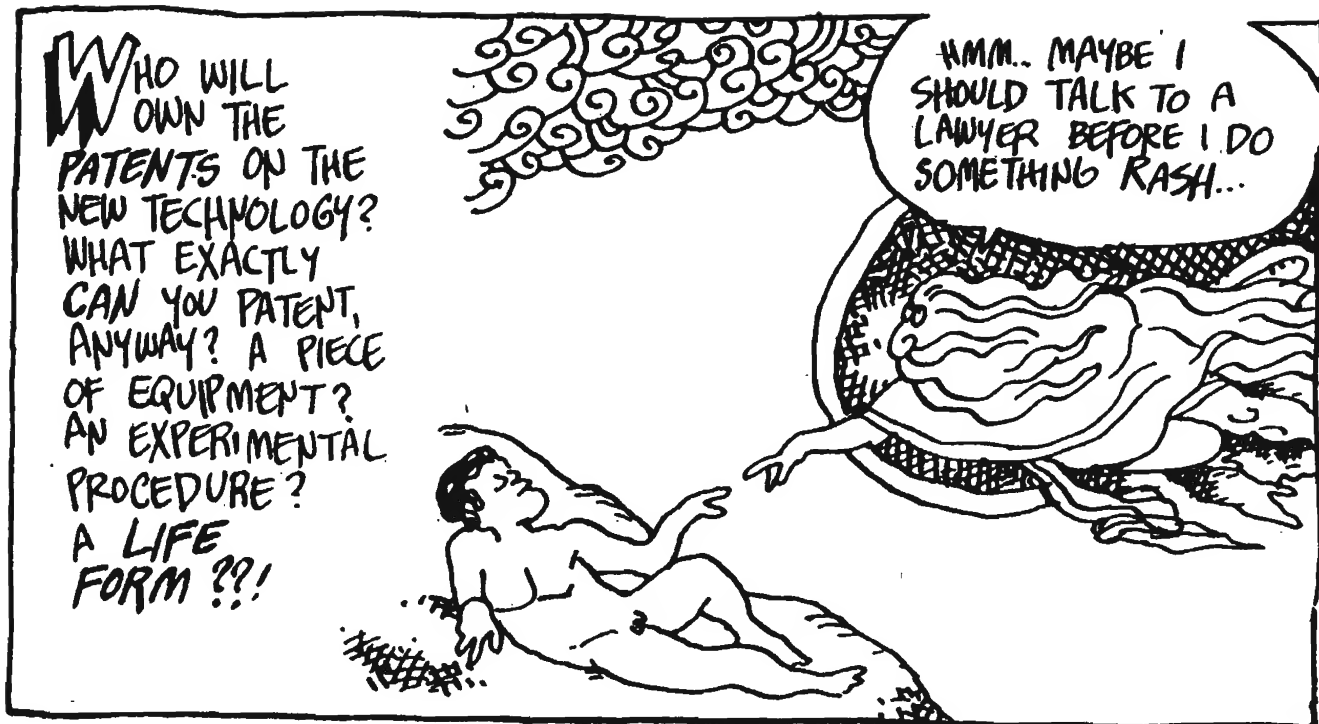
WHERE DO
I GET MY HANDS
DIRTY??

... WHICH HASN'T SLOWED
THE GROWTH OF INDUSTRY
AT ALL!!

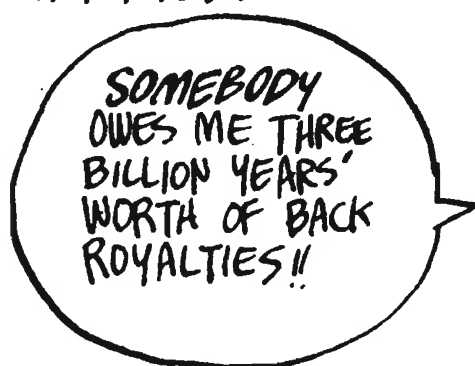
WHERE DO
I GET MY HANDS
DIRTY??

A black and white cartoon illustration. In the foreground, a person is lying face down on the ground, motionless. Their arms are outstretched, and their legs are slightly bent. Above the person's head is a large speech bubble containing the text "YES... WHERE'S THE AMBULANCE?". To the right of the person, there is a small, stylized explosion or crash, with several small circles and lines indicating motion or debris. The background is simple, with some horizontal lines suggesting a ground surface. The overall style is that of a classic comic book panel.

A black and white cartoon illustration. In the foreground, a person is lying face down on the ground, motionless. Their arms are outstretched, and their legs are slightly bent. Above the person's head is a large speech bubble containing the text "YES... WHERE'S THE AMBULANCE?". To the right of the person, there is a small, stylized explosion or crash, with several small circles and lines indicating motion or debris. The background is simple, with some horizontal lines suggesting a ground surface. The overall style is that of a classic comic book illustration.



THIS QUESTION HAS ALREADY GONE TO THE SUPREME COURT, WHICH RULED THAT NEWLY INVENTED LIFE FORMS MAY BE PATENTED!

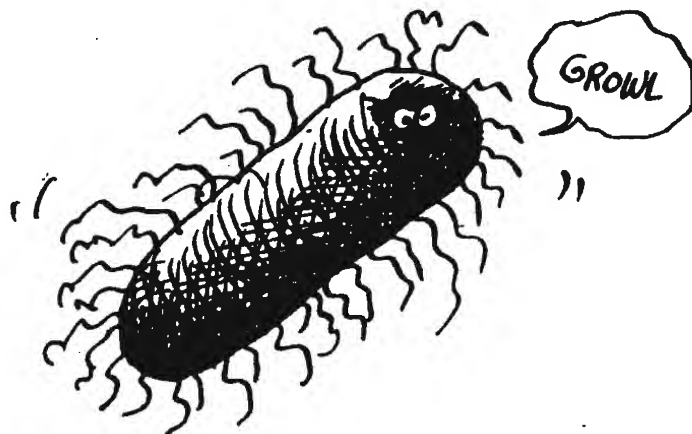


BUT FORGET ABOUT **MONEY**... WHAT ABOUT OUR **HEALTH** ?? FROM THE FIRST DAYS OF GENETIC ENGINEERING, PEOPLE HAVE WORRIED ABOUT BREEDING **MONSTERS** IN THE LAB !!

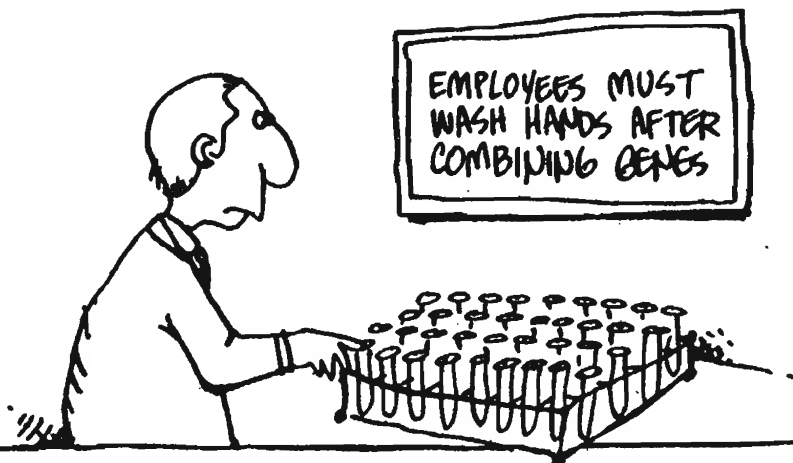


THE FEAR WAS THAT TAMPERING WITH *E. COLI*'S DNA MIGHT CREATE A SUPER-DEADLY GERM BY ACCIDENT.

REMEMBER, *E. COLI* LIVES IN THE HUMAN INTESTINE — IF A VIRULENT STRAIN SHOULD ESCAPE FROM THE LAB, THERE MIGHT BE NO STOPPING IT!! WHO'D HAVE THOUGHT FRANKENSTEIN'S MONSTER WOULD LOOK LIKE THIS?



ACCORDINGLY, SCIENTISTS VOLUNTARILY ADOPTED GUIDELINES TO LIMIT POTENTIAL HAZARDS...



SINCE THE EARLY DAYS,
THE FEAR HAS FADED...
THERE HAS BEEN NO
SIGN OF A PROBLEM
YET!



IT HASN'T
HAPPENED YET,
SO IT CAN'T
HAPPEN AT
ALL!

HMM... SOUNDS
A BIT LIKE
ARISTOTLE...

OR A NUCLEAR
STRATEGIST...

THE MOST ENCOURAGING THING IS THIS: THE STRAIN OF E. COLI
USUALLY USED FOR CLONING GENES HAS GROWN SO "DOMESTICATED"
DURING ITS YEARS IN THE LAB, THAT IT CAN NO LONGER SURVIVE
IN THE HUMAN GUT!!



WE'VE CREATED
A WIMP!!

:-SIGH:-
WE CAN
NEVER GO
HOME...

SO MAYBE, THERE'S NOTHING TO WORRY ABOUT...
THOUGH IT'S TRUE THAT THE SAFEGUARDS
ADOPTED BY UNIVERSITIES DON'T GENERALLY APPLY
TO PRIVATE COMPANIES!!!

WHAT'S MUCH MORE LIKELY
IS THAT SOMEONE WILL MAKE A
DEADLY GERM ON PURPOSE.
WHO WOULD WANT TO DO
THAT, YOU ASK?

I CAN'T
IMAGINE!!!



THE GENERALS HAVE BEEN KNOWN TO TURN NEW
TECHNOLOGY TO MILITARY USE, AND
THEY USUALLY FIND SCIENTISTS
TO OBLIGE...

REPEAT AFTER
ME: "IT'S PURE
RESEARCH!"

IT'S... PURE...



WE CAN TAKE SOME COMFORT FROM THE FACT THAT BIOLOGICAL WARFARE IS BANNED BY INTERNATIONAL TREATY, BUT YOU NEVER KNOW...



LET ME TELL YOU ABOUT SOME BROKEN TREATIES!

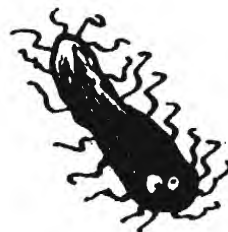
IT'S A POLITICAL QUESTION RAISED BY A SCIENTIFIC ADVANCE — A FAMILIAR FACT OF 20TH CENTURY LIFE.

DOES THIS POTENTIAL FOR HARM MEAN THAT GENE SPLICING SHOULD BE STOPPED?? ALMOST WITHOUT EXCEPTION, THE BIOLOGISTS SAY "NO." WHY REJECT THE MEDICAL ADVANCES ALONG WITH THE MILITARY USES??

BESIDES, THE POISONS THAT COULD BE MADE THIS WAY ARE PROBABLY NO WORSE THAN THE ONES THAT ALREADY EXIST, WHILE MEDICAL ADVANCES PROMISE TO BE TRULY REVOLUTIONARY.



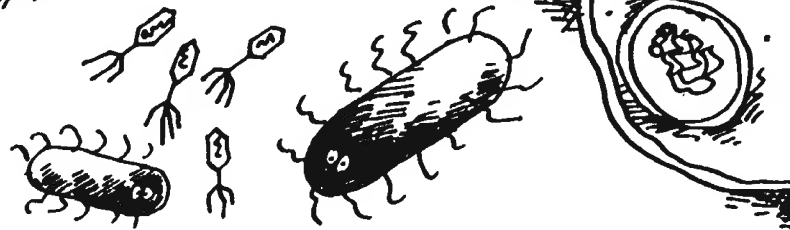
FORWARD!



YEAH... LET US REALIZE OUR HUMAN POTENTIAL...



ON THE VERGE



SO FAR, THE SUCCESSES IN THIS FIELD HAVE COME IN VIRUSES, BACTERIA, YEAST, AND PLANTS, BUT WE'RE GETTING MUCH CLOSER TO WORKING DIRECTLY WITH **HUMAN BEINGS**.

GAK!

HUMANS?

DISGUSTING!



WHEN MAKING TESTS ON HUMANS, SCIENTISTS MUST APPLY A **DIFFERENT STANDARD** FROM THAT GOVERNING EXPERIMENTS ON ANIMALS OR BACTERIA.

NAMELY,
IT'S SUPPOSED
TO DO THE
SUBJECT
SOME GOOD!



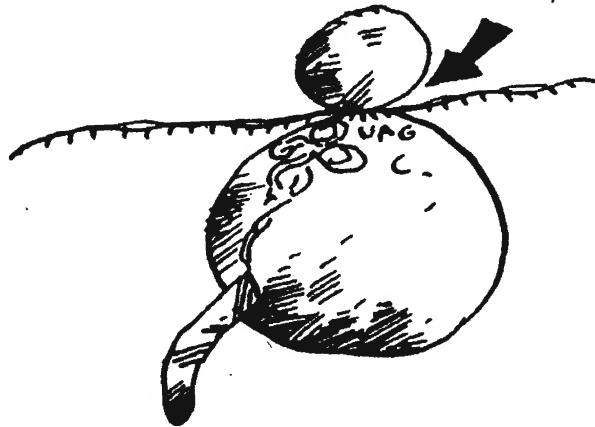
THAT'S WHY WE KNOW SO WELL WHAT CAUSES CANCER IN RATS... HOW COULD YOU DO AN EXPERIMENT TO FIND THE CAUSES OF CANCER IN **HUMANS??**

ASK FOR
VOLUNTEERS?

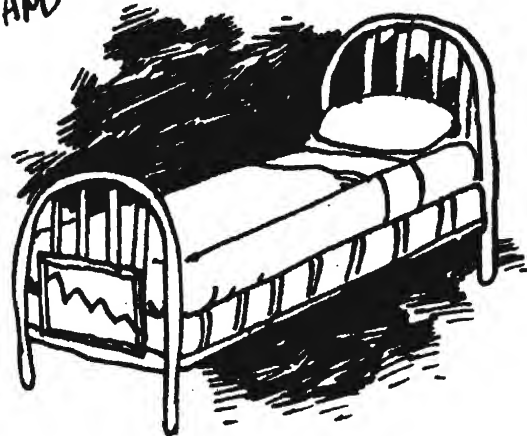


WHICH IS TO SAY, EXPERIMENTS ON HUMANS STIR UP CONTROVERSY, A GOOD EXAMPLE BEING RECENT ATTEMPTS TO TREAT THALASSEMIA.

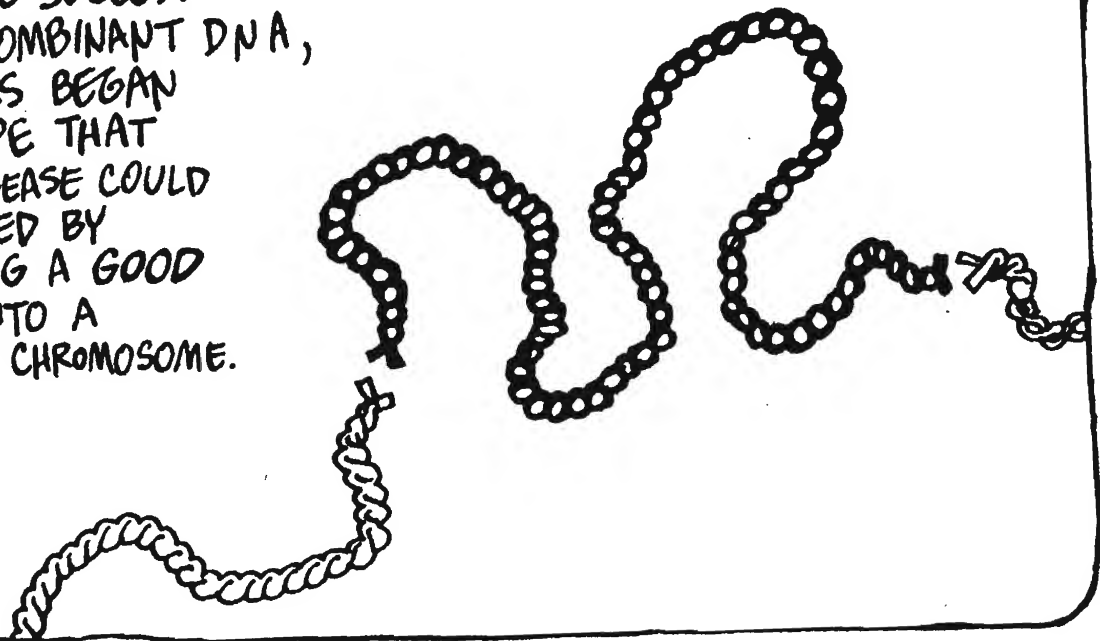
AS YOU RECALL, THIS CONDITION IS AN INABILITY TO MAKE HEMOGLOBIN, CAUSED BY A MISTAKEN "STOP" CODON IN THE MIDDLE OF THE GENE FOR ONE OF ITS CHAINS.



THALASSEMIA VICTIMS CAN SUFFER FROM ANEMIA, BONE DEFORMITIES, AND HEART PROBLEMS. THEY REQUIRE FREQUENT BLOOD TRANSFUSIONS TO SURVIVE, AND EVEN THEN THEY DON'T LIVE LONG.



WITH THE SUCCESS OF RECOMBINANT DNA, DOCTORS BEGAN TO HOPE THAT THE DISEASE COULD BE CURED BY SPLICING A GOOD GENE INTO A HUMAN CHROMOSOME.

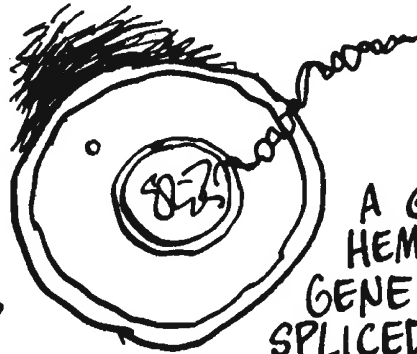




SOUNDS GOOD, EXCEPT THAT THE SAME APPROACH HAD ALREADY FAILED REPEATEDLY IN MICE. STILL, A TEAM OF DOCTORS FROM U.C.L.A. DECIDED TO TRY IT ON HUMANS ANYWAY..!

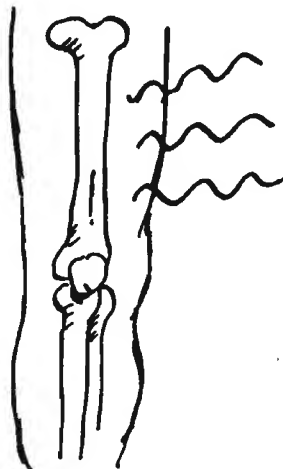


THEY REMOVED BONE MARROW CELLS FROM TWO PATIENTS' THIGH BONES. (REMEMBER, THESE DEVELOP INTO HEMOGLOBIN-PRODUCING RED BLOOD CELLS.)



A GOOD HEMOGLOBIN GENE WAS SPLICED IN.

THE THIGH WAS IRRADIATED TO SLOW DOWN THE OLD MARROW (AND GIVE THE NEW CELLS THE EDGE).



AND THE "ENGINEERED" CELLS WERE PUT BACK IN.



AND THE RESULT?

➡ ABSOLUTELY NOTHING!

(SINCE THEN, THE EXPERIMENT HAS WORKED — IN MICE.)

“SIGH: THERE GOES THE EXPERIMENT...”



AND THE PATIENT...

THE DOCTORS TOOK A LOT OF FLAK FOR THIS EXPERIMENT.



SEVERAL OBJECTIONS WERE RAISED:

NOT EVEN A PART OF THE PROCEDURE HAD EVER WORKED IN ANIMALS. IT'S STILL NOT AT ALL CLEAR HOW TO INSERT A HUMAN HEMOGLOBIN GENE INTO A MAMMAL CELL IN SUCH A WAY THAT IT'S EXPRESSED IN ANY QUANTITY.

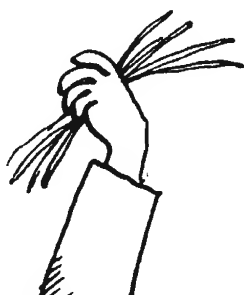
REGULATION IN MAMMALS IS STILL MURKY!

THE EXPERIMENT WAS **DISAPPROVED** BY U.C.L.A.'S COMMITTEE ON HUMAN SUBJECTS USE. HOWEVER, IT HAD BEEN APPROVED BY THE TWO HOSPITALS WHERE IT WAS CARRIED OUT (IN ITALY AND ISRAEL).



THE RADIATION CERTAINLY DIDN'T HELP THE PATIENTS. ON THE OTHER HAND, THEY BOTH FULLY UNDERSTOOD WHAT WAS BEING DONE, AND THEY GAVE THEIR CONSENT.

WERE THEY GRASPING AT STRAWS?

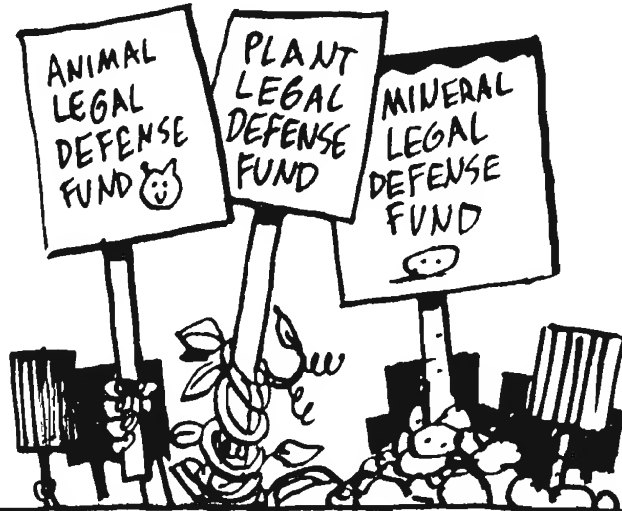


AFTERWARDS, THE DOCTORS WERE DISCIPLINED, ONE OF THEM LOSING HIS POSITION AS DEPARTMENT CHAIRMAN... SO YOU SEE — HUMAN EXPERIMENTS CAN BE DANGEROUS!

DANGEROUS TO DOCTORS, THAT IS!



OF COURSE, THERE ARE FEWER RESTRICTIONS ON PLANT AND ANIMAL EXPERIMENTS THAN ON HUMANS. (THIS BOTHERS SOME PEOPLE, BY THE WAY.)



SO PROGRESS HAS BEEN MORE RAPID AMONG PLANTS AND ANIMALS. ALREADY THERE ARE BREEDS OF COTTON, TOMATO, AND TOBACCO WITH AN ADDED BACTERIAL GENE THAT MAKES THEM POISONOUS TO INSECTS.



SCIENTISTS ARE EXCITED ABOUT TRANSGENIC ANIMALS — ANIMALS THAT CONTAIN A FEW GENES FROM ANOTHER SPECIES.



ONE EXAMPLE ARE PIGS WITH BOVINE GROWTH HORMONE. THEY GROW FASTER AND LEANER, BUT ALSO HAVE OTHER PROBLEMS, LIKE ULCERS AND ARTHRITIS — SO YOU'LL HAVE TO WAIT FOR THAT "BORK" CHOP.



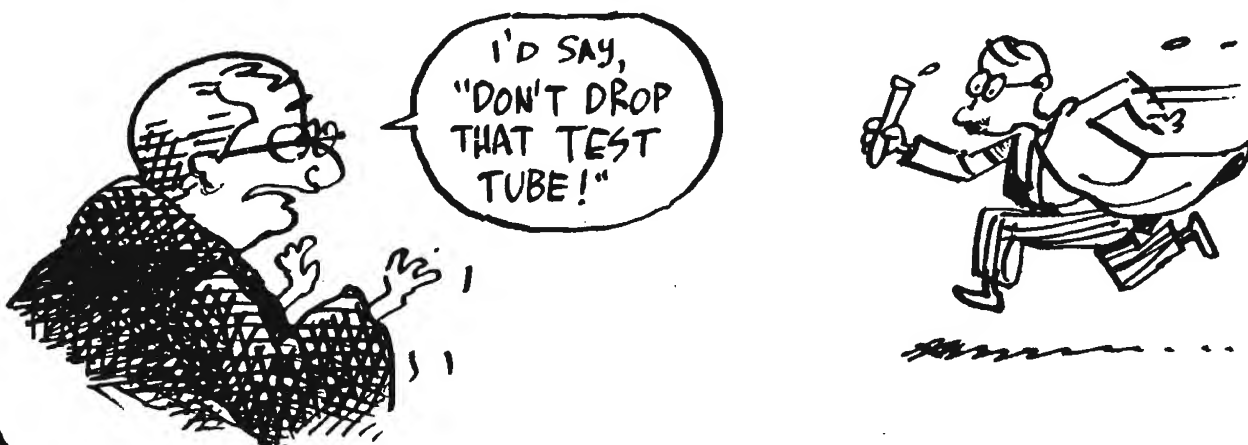
TRANSGENIC PLANTS AND ANIMALS CAN PASS ON THEIR NEW GENES TO THEIR OFFSPRING, BECAUSE THE GENES ARE INSERTED AT A VERY EARLY STAGE OF DEVELOPMENT, ALLOWING THEM TO GET INTO SPERM AND EGG CELLS. PERFORMING THESE EXPERIMENTS ON HUMANS WOULD THEREFORE RAISE SOME HARD ETHICAL ISSUES.



BUT WE'RE GETTING CLOSER. THERE ARE ALREADY LIVING "TEST TUBE BABIES" — FERTILIZED IN A TEST TUBE AND THEN, AFTER A FEW DIVISIONS, IMPLANTED IN THE MOTHER'S WOMB, WHERE THEY DEVELOPED NATURALLY.

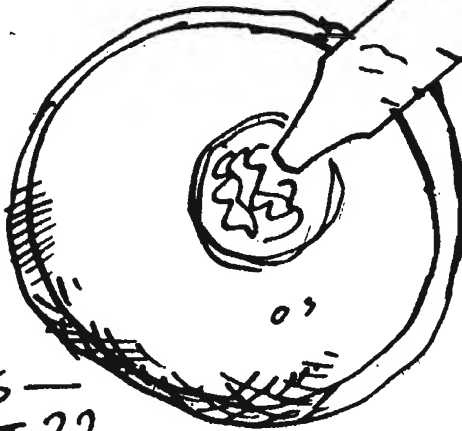


WHAT WOULD THE MONK MENDEL HAVE TO SAY ABOUT **THIS?**

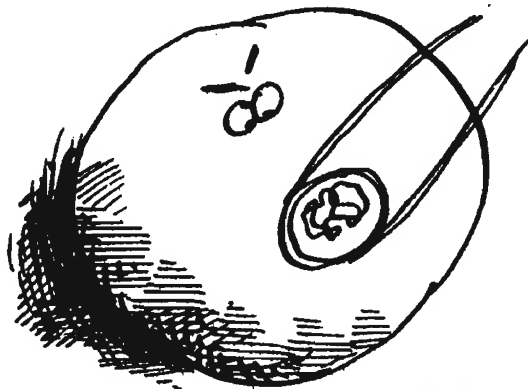
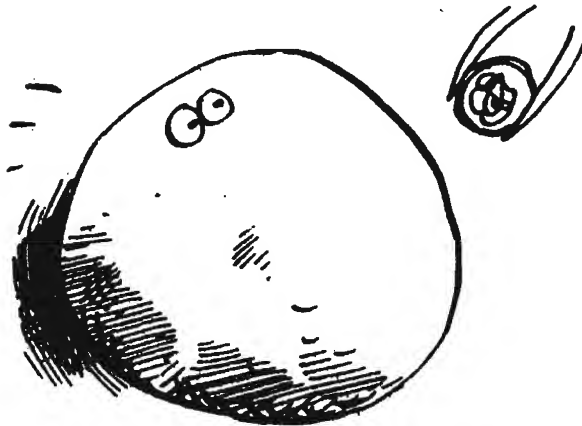


THE OBVIOUS NEXT STEP
WOULD BE TO ENGINEER
THE EMBRYO IN THE
TEST TUBE...

THIS COULD RANGE FROM
GENE THERAPY —
FIXING SPECIFIC DEFECTS —
TO... WHO KNOWS WHAT ??



AT THE EXTREME, IT MAY BECOME POSSIBLE TO **CLONE PEOPLE**. THE EGG'S NUCLEUS WOULD BE REMOVED ALTOGETHER AND REPLACED WITH A NUCLEUS FROM ANOTHER PERSON.



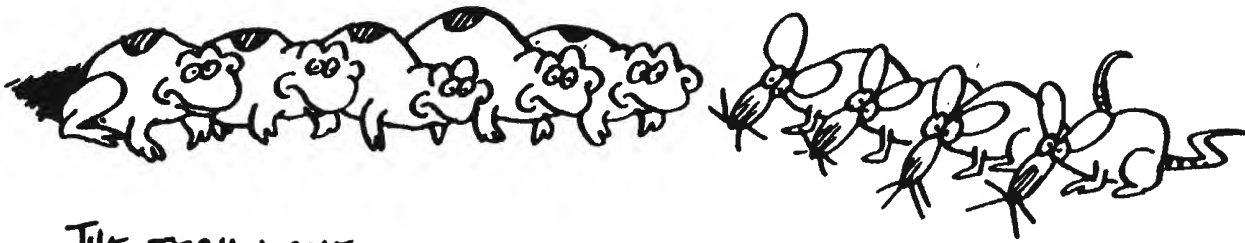
THIS EGG
WOULD BE
IMPLANTED
IN A
"MOTHER,"
TO WHOM
IT WOULD
BE GENETICALLY
UNRELATED.



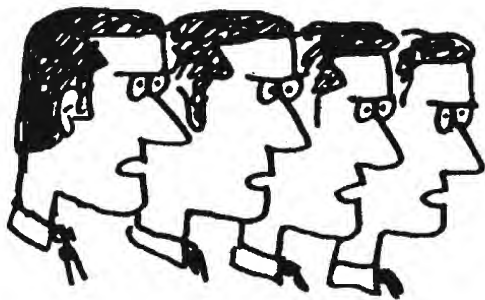
INSTEAD,
THE LITTLE
TYKE
WOULD BE
GENETICALLY
IDENTICAL
TO WHOEVER —
OR WHATEVER —
DONATED
THE NUCLEUS.



SOUND FAR-FETCHED? WELL, SCIENTISTS HAVE ALREADY SUCCEEDED IN CLONING MICE AND FROGS...



THE TECHNIQUE MAKES IT POSSIBLE TO MAKE MULTIPLE COPIES OF LIVING INDIVIDUALS! IS THIS WHAT WE WANT TO BECOME, A WORLD OF CLONES??



WE SEE NOTHING WRONG WITH IT!

YOU MIGHT WELL ASK:
WHO WILL BE CLONED?
WHO WILL DECIDE? WILL
IT BE BASED PURELY ON
MONEY? WILL IT BE LEGAL?
WILL THERE BE PEOPLE-
BREEDERS SELECTING THE
MOST "FIT" FOR REPRODUCTION?

STAND ASIDE,
WEAKLINGS!



THE LAST TIME ANYONE TRIED TO BREED A MASTER RACE, IT WAS AN UNHAPPY EXPERIENCE, TO SAY THE LEAST...

OR MAYBE WE'RE BEING TOO GLOOMY... MAYBE THE FUTURE
WILL BE A GLORIOUS TIME WHEN PEOPLE WILL BE
ENGINEERED TO FIT CLOTHES INSTEAD OF VICE VERSA !!



MAYBE
WE CAN
EVEN BE
CLONED TO
RESIST
ECOLOGICAL
DISASTER,
LIKE THE
DEPLETION
OF
ATMOSPHERIC
OZONE !!



IT'S NOT ONLY OUR OWN GENES WE NEED TO WORRY ABOUT... THERE IS ALSO THE GENETIC DIVERSITY OF THE ENTIRE PLANET... (IT LOOKS SOMETHING LIKE A GIANT CELL, DOESN'T IT?)



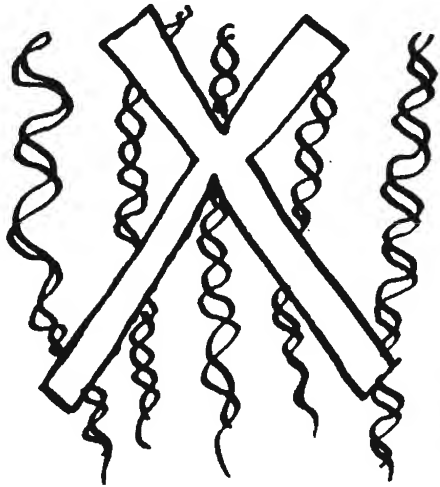
IT'S HARDLY NEWS THAT ALL LIFE IS INTERDEPENDENT... GORILLA EATS BANANA; BANANA EATS CHEMICALS FROM THE SOIL; SOME OF THE CHEMICALS GET THERE FROM BACTERIAL ACTION; OTHER BACTERIA AID THE APE'S DIGESTION; STILL OTHERS BREAK DOWN ITS WASTE PRODUCTS, ETC ETC ETC...



BUT WE HUMANS

WITH OUR EXPLODING POPULATION, RESOURCE-HOGGING, MODERN AGRICULTURE, AND POLLUTION, ARE CHANGING THE ENVIRONMENT SO DRASTICALLY THAT HUNDREDS OF PLANT AND ANIMAL SPECIES GO EXTINCT EVERY YEAR.

THAT MEANS FEWER AND FEWER DIFFERENT GENES REMAIN IN THE BIOSPHERE. ONCE GONE, THEY'RE GONE FOREVER!



I DIDN'T MEAN TO DO IT!



THIS INCREASINGLY THREATENS LIFE AS A WHOLE...

FOR EXAMPLE, IF THERE ARE ONLY 5 KINDS OF APPLE, THEY MAY ALL BE WIPED OUT BY A VIRUS OR BLIGHT...

WHEREAS, IF THERE WERE 50 VARIETIES, CHANCES ARE BETTER THAT SOME OF THEM WILL BE RESISTANT AND SURVIVE.



HOW DO YOU LIKE THEM APPLES?



SEVERAL COUNTRIES ARE ADDRESSING THIS PROBLEM, SAVING AS MANY PLANTS AS POSSIBLE BY COLLECTING THEIR SEEDS.

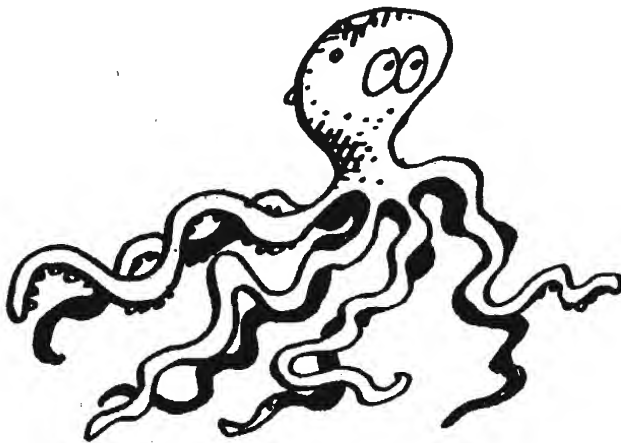


UNFORTUNATELY, THERE'S NO SUCH WAY TO SAVE ANIMALS.

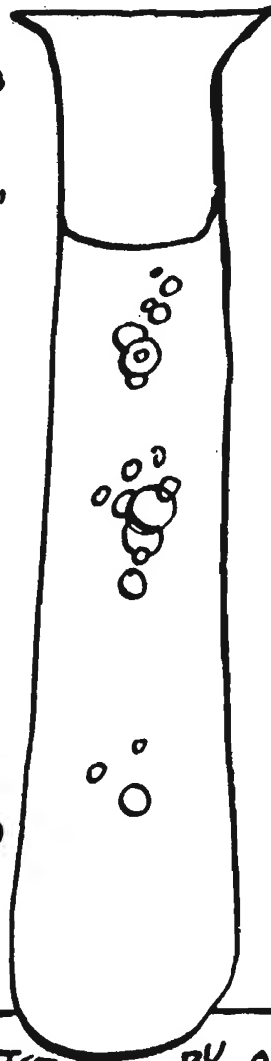


PERHAPS GENETIC ENGINEERING
WILL BE ABLE TO HELP BY
CREATING NEW COMBINATIONS,
BUT THIS IS STILL IN THE
FUTURE...

SAVE
ME!!



ON THE OTHER
HAND, THE
POSSIBILITIES
FOR GENETIC
ENGINEERING
WILL BE
LIMITED BY
THE LIMITED
NUMBER
OF ALLELES
LEFT TO
RECOMBINE.



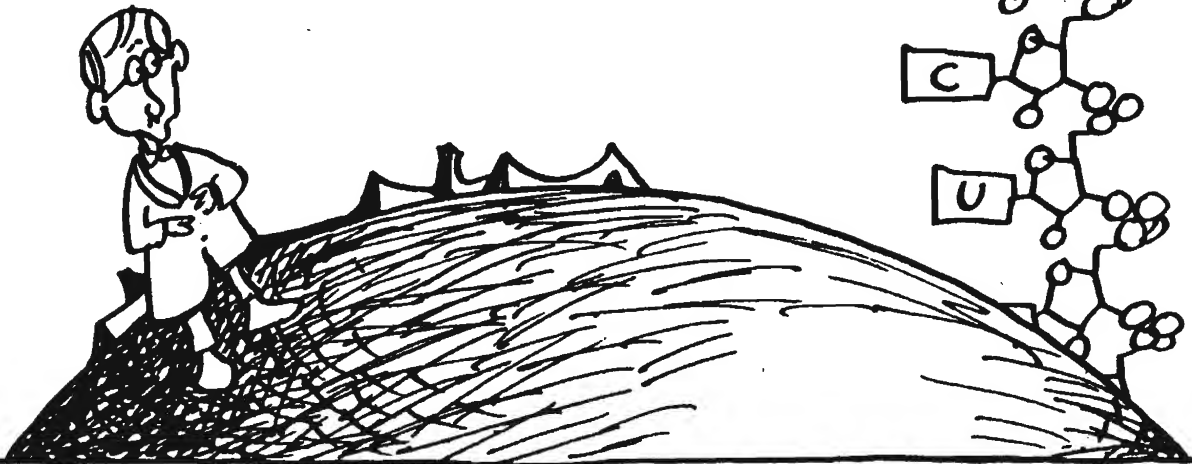
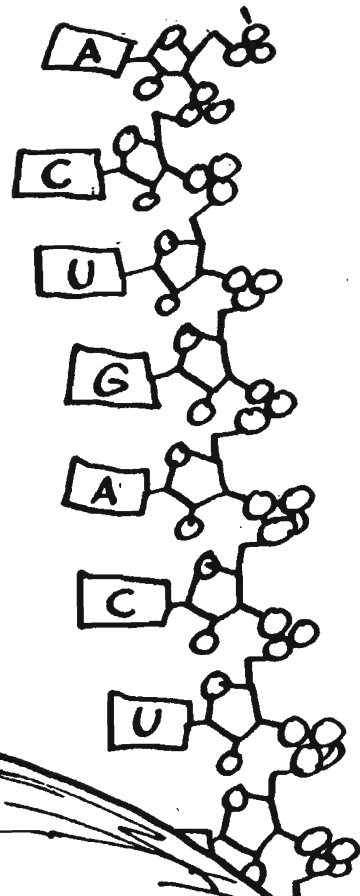
WE FIND OURSELVES CONFRONTED
POWERS.

BY OUR OWN AWESOME

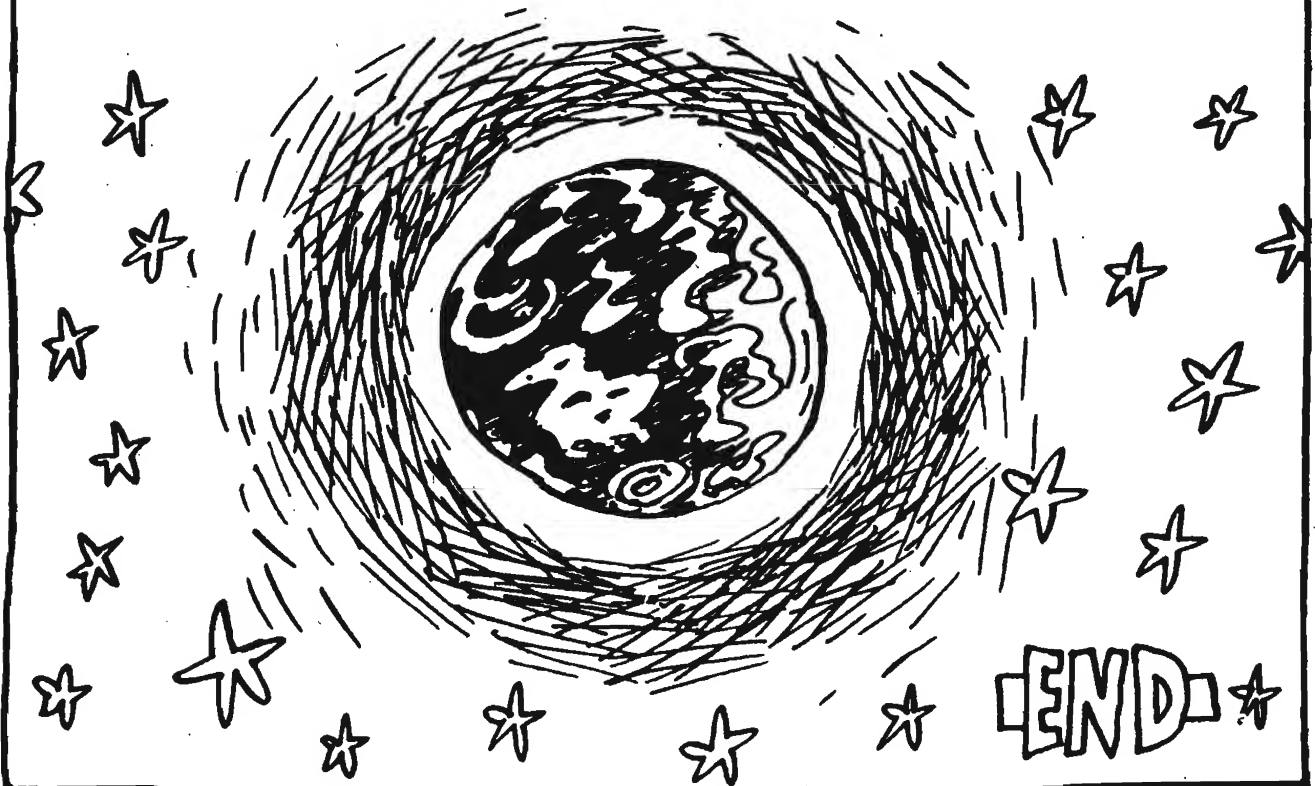
ON THE ONE
HAND, WE
FACE THE
BLIND POWER
THAT STRIPS
FORESTS, ERODES
THE SOIL,
TURNS
MARGINAL
FARMLAND
INTO DESERT
AND DEPLETES
THE HEALTHY
DIVERSITY
OF THE
GENE POOL...



ON THE OTHER HAND, WE MUST DEAL WITH THE GROWING POWER OF GENETIC ENGINEERING. IT PROMISES — OR THREATENS — TO ALTER THE VERY NATURE OF HUMANITY. IT RAISES QUESTIONS WHICH WE BARELY HAVE A VOCABULARY TO DISCUSS, MUCH LESS SOCIAL AND POLITICAL INSTITUTIONS TO DECIDE.



WITH POWER COMES THE RESPONSIBILITY OF CHOOSING WISELY. IN PART, THIS DEPENDS ON ACCURATE INFORMATION. IN A SENSE, WE HAVE COME FULL CIRCLE, TO A TIME WHEN EVERYONE MUST BE A BIOLOGIST, AND THE WORLD IS A CLASSROOM!



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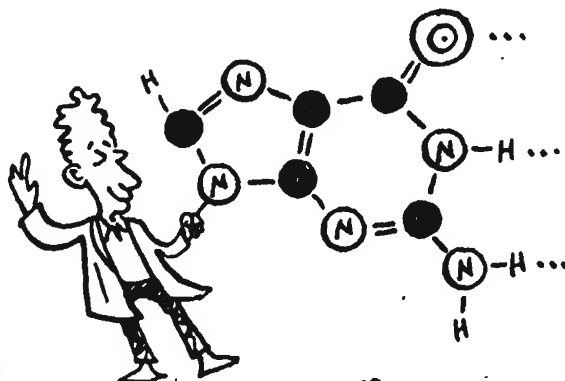
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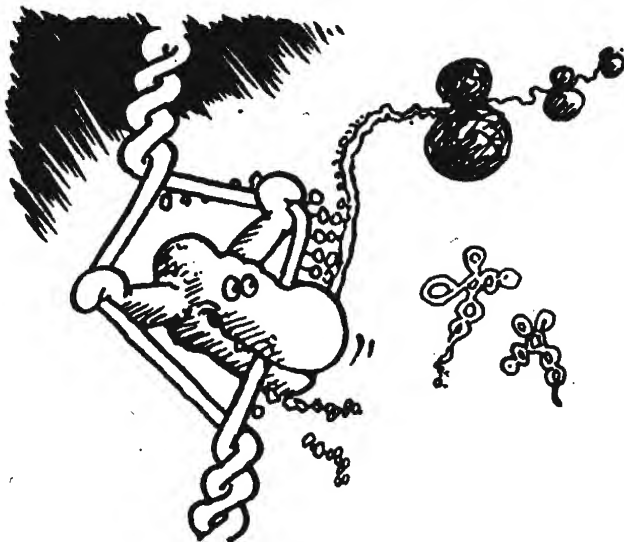


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ALSO: **SCIENTIFIC AMERICAN** MAGAZINE REGULARLY PRINTS ARTICLES ON RECENT DEVELOPMENTS, AND SO DOES YOUR DAILY NEWSPAPER!

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